8

RECORD

7530-222-3525
FEDERAL SUPPLY SERVICE
(GPO)

Book 8

W. Rall

Bldg. 31
Rm 9-A-17

Office of Mathematical Research
National Institutes of Health
Bethesda, Md.
20014

Home ~~telephone~~ WH-6-4455

Home address 11420 LUXMANOR RD.
ROCKVILLE, MD.
20852

Book 8

Research & Computation Diary

Continued from Book 7 on 12/15/65

Past few months have been very active computing with SAAM 22 (Berman program)

Produced several summary charts not in book 7
See p. 30 of this book for recap & stock taking.

12/15/65

Received computer output of 10 decks put in late 12/13/65

$T^* = .092$

655.169 TRNSG, old series, but with monitoring of current p. 181 book 7

Cpt. 16 is a summer which monitors synaptic current in ⑥

17 " " " other " (~~[illegible]~~) ⑥

18 " " " net current into ① from ②

in ① peak not quite reached by max $T = .45$

in ⑥ peak $= .279359$ at $T = .19$

⑯ peak synaptic current $= 7.83$ at $T = .07$ drops gradually

⑰ other current from ⑥ peaks at ~~-1.36 at $T = .05$~~
~~$+3.54$ at $T = .4$~~ $\sigma_{17,6}$ should be $-51.$

⑱ net current into ① from ② peaks ~~at~~ $.3721$ at $T = .27$

last only ⑰

655.149 $\sigma_{17,4}$ should have been $-51.$

in ① peak $= .10$ at $T = .44$

④ .162186 .20

⑯ 4.42266 .08

⑱ peak $= .488$ at $T = .17$

655.554 found $J = 253.764$ in ⑤

to give ipsp peak $= -.05025$ in ① at $T = .58$

peak in ⑤ was $-.09266$ at $T = .14$

645.121 $T^* = .04$ found $E = 4.4078$ in ②

makes epsp peak $= .10$ in ① at $T = .16$

peak in ② was $.11216$ at $T = .11$

However, I don't seriously believe $\lambda_{0,4} = 80.23$; I used this case because I had the necessary I.C. from a previous J run & could get steady state values for reduced R_N. Presumably, a non rect. ought to be roughly proportional to the electrotonic spread voltages, although one could assume a completely uniform Rm change.

12/15/65

645.100 to find peak
used $\varepsilon = 33.64$ in ⑩
got peak in ① $= .058455$ at $T = .86$
⑩ $= .63$ $.09$

645.180 used $\varepsilon = 17.07$ in ⑧
got peak in ① of $.05154$ at $T = .73$
⑧ of $.31994$ $T = .09$

655.910 TRNS $\varepsilon + J$ in ① using old TRNS $T^* = .092$
put $\varepsilon = 1.75 = \lambda_{0,16}$
put $J = 13.87 = \lambda_{0,15}$

got peak $= .0124$ at $T = .19$ whereas ε alone goes $.10$ at $T = .22$
J alone got $-.05$ at $T = .20$

655.940 TRNS $\varepsilon + J$ in ④ put $\varepsilon = 5.01$
$J = 72.24$

got peak $= -.014608$ in ① at $T = .45$

peak in ④ is $-.022438$ at $T = .16$

652.230 need to measure $\varepsilon = 6.6$ in ③ TRNS distort 12% at $T = .29$
St. St. " 30%

654.119 Square ε plus Anom Rect. in ④ $\lambda_{0,4} = 80.23$
in ① Making RN reduced by 42%
peak in ⑪ summer comes out .107
which is pretty close to objective.
Need to check rate of rise.
significantly increased.

Kay remarked that many readers would at first be repelled by the large E values I postulate in the periphery.

My reply is that this is a reaction one probably should anticipate by pointing to the large E factor implied by Action Potential Data -

Phil also mentioned neuromuscular jcn

One further point: I need less E when the area is increased. K likes to consider larger areas.

12/16/65

Worked up three comparisons between slow & fast E transients, these were in cpts ① and ④ of chain of five, & cpt ② of chain of ten. Presented in discussion with K., Phil & Bob Burke. Also presented the EJ results & the anom rect. ~~results~~.

12/17/65 recap.

K discussed the plan of four ?five papers. Originally, the idea had been ⓐ impedance paper methods & results with brief discussion ⓑ anom rect. paper methods & results with brief discussion, ⓒ my theoretical simulation results, ⓓ a joint paper pulling it all together. Now also have Bob Burke's, in which he presents (i) interaction, usually almost linear, which he now takes to mean either (a) near soma (firing results) or (b) electrical isolation (separate branches), (ii) shape of evoked epsp, common features as well as slope differences, (iii) miniatures showing enough variation between themselves to suggest different locations, (iv) repeating single afferents which indicate consistency of temporal dispersion aspect for a single cluster (v)?

K said that he did not believe discussion could all be deffered to joint paper. We agreed that the main thrust of each paper would have to be brought out in that paper. He asked that we start to outline the joint paper. Problem begins to arise about how much overlap there will be in the several discussions. I am beginning to suspect that I should begin to work hard on my own paper — it may turn out that the joint paper will be scrapped & replaced by cross references between the papers. Actually, my original suggestion had been with regard to the electrical versus chemical part of the story. But the most fruitful thing may be cross-referencing between the separate papers. Their original concern, of course, was need for the simulated results. My concern, now, should be to write these up as briefly as possible & to list a full summary of all the conclusions that could be drawn from these simulation studies. At this time, I should do only those additional computations that are really needed.

Previous theoretical studies have ~~provided~~ presented ~~quantitative~~ ~~comparisons of~~ computed ~~simulated~~ synaptic potentials that would be expected at a neuron soma, ~~for~~ in response to ~~a simulated~~ a square conductance change

(from notes dated 12/27/65)

Predictions & generalizations from the computed effects of synaptic conductance change at different soma-dendritic locations.

Synaptic potential computations for various - - -.

Characteristics of synaptic potentials computed for various soma dendritic distributions of membrane conductance change.

Distinguishing between synaptic potentials generated at different locations.

Distinctions between

12/17/65

Kinds of results to be presented

Assume absence of anomalous rectification

I (A) linearity from 0.10 to 0.20 epsp approx near soma, off farther out.
(B) linearity of EJ poor when at common site, better when separated into opposite trees.

(C) Shape constancy is shown by my plots.
II (D) change in slopes with pert location
" " various Δt
also peak in the remote location.

III Observability of Conductance change

IV Compare time course of $\mathcal{E}$, of synaptic current, of V at pert. cpt. ~~and~~ of soma-dendritic current, and of epsp at soma.

Possible titles

Quantitative Study of Simulated Synaptic Potentials.

~~Effect of~~

Dendritic location effect upon computed synaptic potentials locations

Effects of different soma-dendritic locations upon ~~the~~ computed responses to synaptic conductance changes.

Insights obtained from computed synaptic conductance changes at different soma-dendritic locations.

Predicted Effects at Soma of computed for ~~various~~ various ~~[illegible]~~ synaptic conductance changes at various soma-dendritic locations.

~~Took~~

10

12/17/65

Received Walter Freeman's manuscript – glanced at it, but haven't strength to study it now. Felt like opening Pandora's box.

Perhaps plan to prepare most essential decks for further calcs. First, check one point already available.

? Do the epsp of the 556 series have the same time course as the net distortion (Gt. 18) of the 656 series?

	556.210 epsp	656.210 distort ⑱
time of peak	.40	1.40 − 1. = .40
rising ½ max at	.16	approx 1.15+ − 1. = .15+
falling ½ max at	.99	2.0 − 1. = 1.0
20th going up	.10	~1.10 − 1. = .10

Seem to agree well in shape characteristics

also for pert in ①

now look at pert in ⑤

	556.510 epsp	656.573 ⑱
time of peak	.95	2.0 − 1. = 1.0
~ rising half max	.45+	1.45 − 1. = .45
falling 64%	1.73	2.75 − 1. = 1.75
rising 90% to 10%	.25	1.25 − 1. = .25

also agrees well

* This has very significant consequence: Because this distort. closely follows epsp time course, it very obviously does not represent E time course at all. This is rather different from the A.C. impedance approach which assumes that it can get actual time course of E. Actually A.C. steady state does not exist. I pointed this out to K. He agrees but says you can follow a slow transient change in impedance & then he says they made use of sidebands of test frequency.

cf. p. 173 of book 7

12/17/65

Have just checked (see pp 187-188 of book 7) the rel. amplitudes of sinusoidal approx steady state against, step at T=1.0. Find the % values are lower for sinusoidal.

Now decided to look at step ~~steady state~~ values for T < 1.0 Values are available for the 5 cpt chains 656 series.

	①	②	③	④	⑤
T=1.0	.2664	.1627	.09808	.06091	.04404
	100	61	37	23	16.5
T=.8	.2466	.1443	.0818	.0468	.03124
	100	58	33	19	12.7
.7					
T=.6	.2197	.1201	.0620	.03117	.01816
	100	55	28	14.2	8.3
T=.4	.1814	.08766	.0383	.01543	.00693
	100	48	21	8.5	3.8
T=.2	.1213	.0432	.01275	.003184	.000796
	100	35.6	10.5	2.6	0.66

	①	③	⑤	⑦	⑨
Chain of 10 T=1.0	100	61	37	22	15

agrees pretty well ~~with~~ when these odd cpts are compared with chain of five.

odd cpts of Sinusoidal p. 187 Book 7	100	55	30	17.5	13

Seems to corresp to about T=.7

see also p. 37-38 below

12/17/65

(12/20/65 – Spend half the day with Dr. Florio interested in Math. Consultancy.)

Decks to prepare

655.009 pair needs appropriate σ set to -51.

also consider plotting scales & Kappas.

645.101	fits	645.101	(12/20/65)
645.181		645.181	(12/20/65)
645.110	to be setup	645.111	(12/20/65)

655.900 EJ could be changed to two chains of five

546.150 to be prepared

646.120 to be resubmitted 646.121 (12/20/65)

646.130 } can now be prepared.
.140 }

65.312 continued sinusoidal. put in I.C. 65.312 (12/20/65)

12/21/65

	I.C. from previous T=6.0	new value at T=6.0	new peak value	at T
1	.07046	.0704823	-.0946235	5.25
2	.04124	.0412607	-.0703772	5.30
3	.02083	.020854	-.052046	5.35
4	.0072638	.00728655	-.038525	5.45
5	-.0012557	-.00123297	-.0285137	5.50
6	-.0062414	-.00621866	-.0213916	5.60
7	-.0089030	-.00888053	-.0165706	5.70
8	-.010157	-.0101345	-.0137182	5.75
9	-.01065	-.0106295	-.0122611	5.85
10	-.01080	-.0107774	-.0116943	5.85

↑

These agree to better than 99% with earlier results on p. 188 of book 7

This halfway slope = .287

12/21/65

65.312 Sinusoidal, values tabulated on p. 14
Appear to be very close to steady state

645.111 cpt ① with fast TRNS $\mathcal{E}$

old $\mathcal{E} = 1.75$ gave epsp peak = .0656 at T = .11
Fit is, however being done at T = .12

.0100695
Found $\mathcal{E}$peak = 2.762 gives epsp = .01 at T = .11
nearly linear
∴ correct to $\boxed{2.74 = \mathcal{E}}$ in ①

Also need to measure slopes.
Slope at rising ½ max is 1.63 $\tau \frac{dV}{dt}$
$\therefore \frac{\tau}{V_m}\frac{dV}{dt} = 16.3$

645.101 cpt ⑩ with fast TRNS $\mathcal{E}$

$\mathcal{E}$peak = 100 was not enough
gave epsp peak = .0847563
at T = .86

in cpt ⑩
peak = .8607 at T = .07

645.181 found $\mathcal{E}$peak = 49.867 in ⑧
gives epsp peak = .1 at T = .73

---

in ⑧ peak = .60245 at T = .08

12/21/65

646.121 three chains. Had card error

put in 646.122
646.130

655.149 } redo with plot
655.169 } & corrected $\sigma = 51.$

Need to measure slopes for Thursday session with others.

12/22/65

put in 645.182 ⑧ more time
645.102 ⑩ larger max E
645.130 new ③

got back top four late on 12/22/65
" " lower three " " 12/23/65

On 12/22/65 did measuring of 645.1 series
and also of 556.1 vs 546.1 series
for a comparison chart.

! Test measurability of conductance change dist uniformly over the whole neuron. !

Also try to simulate Bob Burke's special epsp pair, see notes

Joint paper During discussion with Phil Nelson & Bob Burke today

The overall question is to assess how well the data can be completely accounted for by spatial ~~differences~~ distributions in membrane conductance distribution.

Also, ask if any don't fit — do they point to electrical synapses? Also, how basically different are electrical & chemical synapses.

Sections of Joint paper

I - ΔZ Sensitivity of impedance measurement & influence of dendritic locus
electrical vs chemical
& location

II - ΔR ① variable $\frac{dV}{dt}$ of epsp
② variable effect of polarizing currents on epsp

III PSP ~~interaction~~ & time course
Compartment effect on time course vs. temporal dispersion

Compartmental effect on interaction quantitative.

12/23/65

646.130 – Three short chains with $T^* = .04$
with $\mathcal{E} = 9.52$ peak in ③
at T = .42

std. control (11) .3435548
pert in ① .2624906
.0810642

24.3%

~~peak 18 is .15618~~
control 11 is .294342
~~pe~~ 17 is .283930
true Δ .010412
⑱ is 15 times this
% distortion is 3.54%

646.122 with $\mathcal{E} = 4.2545$ in ②
T = .26

control .3435548
pert .2323766
.1111782

32.4%

control .285327
(17) .268450
(18) .016877

5.91%

655.149 FRNSG Monitor Current
Data points exceed 250 in number.
? card error

655.169B ~~seems OK~~. ran, but plotting scale way off.

in ① peak = .1001	at T = .62		
in ⑥ .27936	.19	×	Kappa = .05587
in ⑯ 7.83	.07	×	.1566
in ⑰ −6.23	.11		−.1246
in ⑱ .3719	.26		.0744

Need to setup

12/30/65

✓645.140 at T = .32 start with ε = 5.01

✓645.160 at T = .50 " 9.86

✓645.102 ⑩ followed out, without fit or plot to

✓661.143 mod of 655.149B Monitor Current

✓661.163 655.169B " "

✓662.001 Three Channels EPSP SUM

(see p. 26)

These did not go in until morning of 1/3/66

12/23/65

645.130 Found $\mathcal{E} = 6.965$ in ③
gives epsp peak = .101139 in ①
at T = .22

peak in ③ is .15514 at T = .09

645.182 goes out to falling half max that
was missed before.

645.102 opt ⑩ ~~found~~ $\mathcal{E} = 150$ in ⑩ reached .0925 in ①
at T = .86

Found $\mathcal{E} = 234.35$ in ⑩
to get .100016 in ①
at T = .86

peak in ⑩ is .9403 at T = .06
peak in ⑭ 1.0 .04

Need more time without fit to get falling half ma

12/27/65

This week, try to concentrate on writing a draft on the simulated experiments for the joint series. — mornings.

Also, in afternoons, catch up correspondence & set up a few more computations. esp. FLD+MG & uniform epsp & measurability of G

12/30/65 Got several letters written

Ito
Kitasato
Brooks
Elias
Obert

12/30/65 set up computation decks — see p. 23.

New series 662. Three Chains EPSP SUMS

$\lambda_{ij}^{ee} = 6.25$

I.C. = 1.0 in ⑯ and 2.71828 in ⑰

$\lambda_{18,17} = \lambda_{0,18} = 25.$

662.001

Wanted E peak = 1 in ② and ⑦

E peak = 5 in ⑤ and ⑮

1st chain has both
2nd chain has ② alone
3rd chain has ⑤ alone

Summing 20, has sum of ⑥ + ⑪

$\lambda_{2,16}$	1.	Q dep on 18
$\lambda_{7,16}$	1.	"
$\lambda_{19,2}$	1.	"
$\lambda_{19,7}$	1.	"
$\lambda_{5,16}$	5.	"
$\lambda_{15,16}$	5.	"
$\lambda_{19,5}$	5.	"
$\lambda_{19,15}$	5.	"
$\lambda_{0,16}$	-12.	"

$\sigma_{20,6}$ 1.

$\sigma_{20,11}$ 1.

Data points in 1., 6., 11., 20.

each 200. .04 55.

based on 65.311

663.031 Two Chains – Pert. Sinus.

$\lambda_{12} = 6.25$ delete λ_{56} & $_{65}$ ✓

I.C. .06 in 1 & 6
.015 in 2 & 7
zero in rest

Monitor 1, 2. 3, 4. 5. starting with T = 2.
200. 2. 3.
giving T = 2., 4., 6., 8.

T.C. 126. ⑫ 1. ㉗ 1.

Let ⑪ take ⑥ - ①
Let ⑫ take ⑧ - ③

starting at T = ~~10.~~ 8.
monitor 1., 6., ~~11.~~ ③ & ⑧ ~~12.~~
200. .05 20.

~~0.~~ 11. & 12. .02 50.

7. 9. 10
200. .1 10.

13 & 14 generate sinusoidal I.C. in ⑬ = 1.

$\lambda_{1,13} = 1.0$
$\lambda_{6,13} = 1.0$
$\lambda_{0,13} = 1.1416$
$\lambda_{0,14} = -3.1416$
$\lambda_{13,14} = +3.1416$
$\lambda_{14,13} = -3.1416$

given $\lambda_{17,3}$ depends on Q_{16}

TRNS G generated after T.C.

then I.C. in ⑮ = 2.71828

all the time $\lambda_{16,15} = 25.$
$\lambda_{0,16} = 25.$

after T.C. $\lambda_{17,3}$ 9.52

28

1/3/66

Setup 546.150 short chain with T^* est. at .81

646.140

546.141 zero iterations with $\varepsilon = 19.6$

663.031 see left

~~661.100~~ 645.100 ~~[illegible]~~

single cpt. see below

(4)

1.

200. .01 50.

100. .15 .01 /

1. .15 .1

100. /

let I.C. = 1. in ② be E_C

I.C. = 2.71828 in ③

$\lambda_{4,3} = 25.$

$\lambda_{0,4} = 25.$

$\lambda_{1,2}$ 41

$\lambda_{5,7}$ 41

$\lambda_{0,2}$ 41

G.6 is summer on 2+1

2.

.02

$\lambda_{0,5} = .2$

$\lambda_{1,2}$ $\lambda_{0,5}$ 1.

$\lambda_{5,2}$ -1.

$\lambda_{0,2}$

1/4/66

Corresponding Charts used in (December 65 discussions) with Phil, K. Frank & Bob Burke

One each for 654.2
654.1
654.5
652.2
652. → 1, 2, 5 combined
655.1
655.5
653.1 & .5 combined
654.108
556 & 656 short chain series
645.1
546.1 versus 556.1 comparison
654.1 versus 655.1 comparison

small graphs
654.100 series
655.100 series

large graphs — tracings

see p. 161 of book 7 { Pert in ①, response in ① square E versus slow TRNS E
⑩ ① " "

Summary

1/4/66

Here we list all of the recent computation series and then go on to survey the summary charts that were prepared during the last two months. Refer also back to p. 60 of Book 7 and to pp. 135 and 146 of Book 7

Square conductance change series

Oct 65 March & Oct 65

654. begun originally as 65.400 out of 65.100

654.200 Square E fit for epsp peak = 0.20 in ①
Done for pert. in 1, 2, 3, 4, 6, 8

652.200 Distortion of Current Step response by above square G values
Done for pert in 1, 2, 3, 4, 6, 8

654.100 Square E fit for epsp peak = 0.10 in ①
see .108 at bottom
Done for pert in 1, 2, 3, 4, 6, 8, 10

652.100 Distortion of Current Step response by these square G values
in 1, 2, 3, 4, 6, 8, 10

654.500 Square J fit for ipsp peak = −0.05 in ①
Done for pert in 1, 2, 3, 4

652.500 Distortion of Current Step response by these square G values

Slow Transient Conductance change series $T^* = 0.092$ see p. 170 book 7

655.100 TRNS E fit for epsp peak = 0.10 in ①
Done for 1, 2, 3, 4, 6, 8, 10

653.100 Distortion of Current Step response by above TRNS G
Done for 1, 2, 3, 4, 6, 8, 10

655.500 TRNS J fit for ipsp peak = 0.05 in ①
Done for 1, 2, 3, 4, 5

653.500 Distortion ~~of~~ Current Step response by above TRNS G
Done for 1, 2, 3, 4

655.108 TRNS E
Done 2, 6,

654.108 Square E upon steady state hyperpol (−.3771) 1, 2, 3, 4, 6, 8

New mathematician in programming section.

Richard Shrager

Rm 2220, Ext. 63626

brought around by Jose

Will build up Fortran IV library.

later phone call from

James Kiefer 66563

interested in programming.

~~658.900 TRNS E+J see pp. 184 of book 7, p. 4 this book.~~

1/4/66 Summary Continued

[illegible] TRNS ~~T* = .04~~

556. series Short (5) Chain - ~~fast~~ slow TRNS E, fit epsp peak = .10

Done 1, 2, 3, 4, 5

656. Three chain method using summers to get distortion

Done 1, 2, 3, 4, ⑤

Medium
~~Fast~~ TRANSIENT E, T* = .04 see p. 170 of book 7

546. series Short (5) Chain TRNS E fit epsp peak = .10

Done 1, 2, 3, 4, ⑤

646. series Three chain method using summers to get distortion

Done 1, 2, 3

645.1 series long Chain fast TRNS E fit epsp peak = .10

Done 1,

655.900 slow TRNS E+J see p. 184 of book 7 & p. 4 here

65.300 New Sinusoidal series with period = 2τ
663. Two Chain - Perturbed Sinusoidal " p. 27

662. New Three Chains - EPSP Sums p. 26

{655.009 Monitor Synaptic & other current (p. 181 book 7)
{661.1 " " (p. 2 this book) p. 23

654.109 Anom. Rect. simulations. (p. 4)

Prepare chart

Now have 645.1 with pert. in ②, ⑧, ⑩, ①, ④, ⑥, ⑬

~~next ③~~

Put in (late 1/4/66)
661.144
661.164
662.002 } with old SAAM 22 which should plot correctly.

1/4/66

This afternoon, finally got back results setup 12/30/65 - seep. 23

645.140 TRNS G Mod $T^* = .04$

initial $\mathcal{E}$peak of 5.01 in ④ gave .0524 in ① at T = .29

found $\mathcal{E} = 10.60$ in ④ .1007 T = .29

peak in ④ is .22 at T = .09

645.102 run of $\mathcal{E} = 234.$ in ⑩

got epsp = .0999$_{26}$ in ① at T = .86

ample run time

645.160 initial $\mathcal{E}$peak = 9.86 in ⑥ gave .0504 in ① at T = .47

found $\mathcal{E} = 24.39$ in ⑥ .1004$_2$ T = .47

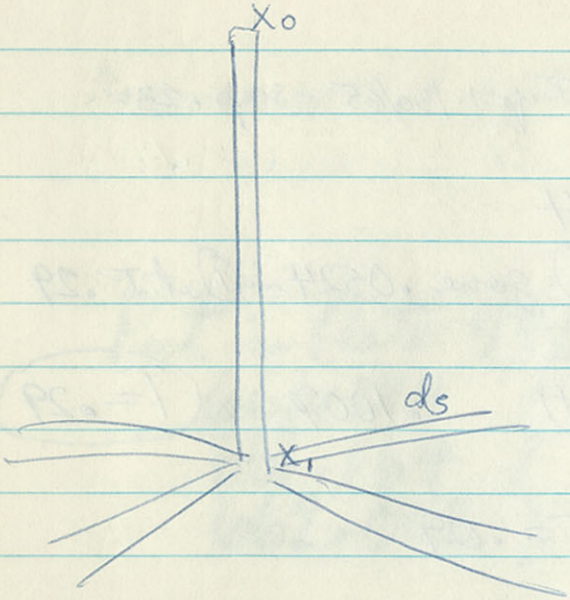
peak in ⑥ is .4054 at T = .08

661.143 Slow TRNS $\mathcal{E}$ — Monitor Current.
661.163 old 655.109 series " "

→ Two problems $\sigma_{17,4}$ & $\sigma_{17,6}$ got interchanged by mistake
also, plotting subroutine misbehaving.

662.001 Three chain epsp sums. fast TRNS
for $\mathcal{E} = 1$ in ②
$\mathcal{E} = 5$ in ⑤

goofs in setup



This point was discussed with Pollen & Lux for their pyramidal cells.

Also, this point was, I believe, neglected in the Kitasato paper.

This should be dealt with in my review
Could refer back to slide that was
use for my 1958 Fed. Proc.
presentation.

1/5/66

Spent much of day ~~preparing~~ going over Gordon's material & writing him a letter, catching up & commenting on his review with Ottoson

Did following calculation for steady state electrotonic decrement from olfactory glomerulus to mitral soma

Use Eq. 3 of 1959 paper $\frac{V_0}{V_1} = \cosh(L_0/\lambda_0) + B_1 \sinh(L_0/\lambda_0)$

with directions reversed: ie X_0 = glomerulus

X_1 = soma

and $$B_1 = \frac{\sum d_s^{3/2} \tanh(L_s/\lambda_s)}{d_0^{3/2}}$$

d_0 is primary dendrite diameter

Where numerator represents the secondary dendrites.

Suppose $L_s/\lambda_s = 1.0$, that $d_s = \frac{1}{2} d_0$ & that $N_s = 4$

Then $$B_1 = \frac{4(.76)}{2^{3/2}} = \frac{3.04}{2.83} = 1.075$$

$$= \sqrt{2}(.76) = 1.075 \quad \approx 1.0$$

But, if $d_s = d_0$, then get $B_1 = 3.04 \simeq 3.$

Then, for $L_0/\lambda_0 = 1$, get $\frac{V_0}{V_1} = 1.543 + 3(1.175) = 5.07$

compared with 2.718 for $B_1 = 1$

And for $L_0/\lambda_0 = 1/2$, get $\frac{V_0}{V_1} = 1.128 + 3(\overset{1.562}{.5211})$

$= 2.69$ compared with 1.65 for $B_1 = 1$

663.031
645.001
646.140
546.141
546.150

663.032
645.001B

rel amplitudes
100
54.8
30
18.2
14.3

refer back to
page 12
agrees

Set up 663.032
with new I.C. set as T=8.0 values at right

1/6/66 Morning on sick leave
Afternoon, go over recent computer output.

663.031 Two chain pert. sinusoidal worked, but next time have less than 250 data points

Found steady state values

	T=8.0	extremum
1&6)	.1097	.16288 at 8.25
2&7)	.02788	.08931 at 8.40
3&8)	-.00681	.04906 at 8.55 .30
4&9)	-.01816	.02971 at 8.70
5&10)	-.02058	.02333 at 8.80

fast TRNS E in ③
peak E = 9.52

which in 546.13
caused peak in ③ at T=.10
& in ① at T=.66

Cpt. ⑪ gives control ⑥ - ① of pert chain

early small neg deflection
due to early neg effect farther out

peak occurs at T=8.50
⑪ Δ = .000658

when ⑥ value is .1207

or 0.5 %

Conclusion: the timing was unfavorable here.
Biggest effect should occur for T.C. near 8.55, say 8.50

cpt. ⑫ gives control ⑧ - pert ③

Note that 3&8 are neg at T=8.0
but pos. for all the rest of the time to T=9.0

at 8.05	③ = ±.00132	⑧ = .000877
8.10	.00761	.00854
8.15	.01408	.016
8.20	.02095	.023

from 8.10 on pert ③ is smaller than ⑧
but from 8.0 to 8.08, early reduced neg causes pert ③ to be pos. rel to ⑧.
& hence ⑫ is neg for 8.02-8.06

cpt. ⑫ peaks at 8.20 Δ = .0021
approx 10%

See p. 56 for 661.101

Note: here, single lump
ε peaks at T = .04 (cpt. 4)

Synoptic current peaks at T = .04 (cpt 6)

See if max slope in ① occurs also at this time.

0 to .01 $\Delta V = .0034$
.01 to .02 $\Delta V = .0081$
.02 to .03 $\Delta V = .0104$
.03 to .04 $\Delta V = .011173$ ✓ yes
.04 to .05 $\Delta V = .01096$

Now compare with monitor current
in remote cpts. Now 661. series
see p. 32
p. 44-46

1/6/66 rename 661.100

645.100 single cpt. fast TRNS.

also summer ⑥ monitors synaptic current.

found $\mathcal{E}$peak = 1.19 causes Vpeak = .1032
at T = .20

In this case, time course of synaptic current is very close to time course of conductance change.

neither needs to be followed much beyond T = .30
both peak at T = .04

setup 645.100B for longer time & corrected peak
661.101

646.140 Three short shows with $\mathcal{E}$ = 19.6 in ④
⑱ has factor 1/20
at T = .65

st.st. control ⑪ .3435548 ⑪ goes
st.st. in ① .2901809 ⑰ goes .298048
.0533739
67

⑱ goes .133958
This over 20 goes .0066979
∴ ⑪ must be .30475
and this is 2.2%

15.5%
st.st. distort

546.141 rerun shows $\mathcal{E}$ = 19.6 gives peak = .100129 at T = .65 & .66

1/6/66

546.150 shortchain, fast trans.

found E = 44.573 in ⑤ 44.6

gives epspeak = .099918 in ① at T = .82

peak in ⑤ is .83538 at T = .09

.836

Can now complete table comparing 546.1 & 556.1 for all five expt. positions

* Also, now possible to setup 646.150.

cpt. 18 monitors net current from dendrites to soma.
This peaks at T = .18 - and reverses at T = .6
which looks to be close to max time rate of rise in ①

T = .24	.0698652	Δ = .0073486
T .22	.0625166	Δ = .0080664
.20	.0544502	.0086174
.18	.0458328	.0089178
.16	.0369150	.0088716
.14	.0280434	.0083812
.12	.0196622	

reversal implies that cpt. ② voltage falls faster than cpt ① voltage which is presumably due to equalization time constant effect toward other end.

also, note $\lambda_{11} = 26.$
$\lambda_{22} = 51.$

at T = .08 synaptic in current ⑯ = 4.42266
loss current ⑰ = 3.28679
net current = 1.13587

at T = .04 ⑯ = 3.63464
⑰ = 1.97222
net current = 1.66242 presumably near peak

i.e. steepest slope in ④ occurs not at peak synaptic current, but at peak of difference between ⑯ & ⑰

Compartment ① peaks at T = .44; steepest rise is at T = .16

loss current ⑰ peaks at T = .11, when it is 3.543
This occurs earlier than time of peak in ④ because losses to 3 & 5 reduce as

1/7/66

Yesterday got back 661.144
661.164
662.002

661.144 Slow trans E with Monitor Currents
Can check points raised on pp 39-40
which were really original objective.

Here E in ④ is given by ⑭ which ~~peaks~~ showed at .092 but was not monitored here.

synaptic current in ④ given by ⑯ which peaks near .08
only slightly less at .09

Voltage in ④ peaks at T=.20, value of .1622

~~whereas at~~

T=.13	V=.148208	Δ .005346
.12	.142862	.006496
.11	.136366	.007760
.10	.128606	.009133
.09	.119473	.010600
.08	.108873	.012131
.07	.096742	.013662
.06	.083080	.015090
.05	.067990	.016225
.04	.051765	.016742
.03	.035023	.016056
.02	.018967	.013096
.01	.005871	.00587

slope peak in ④

345

These 661. results
and 645.100, renamed 661.100 p. 39-40
all fit intuition quite
well & could provide
the basis for a figure

T	Rel E value	V_6	$(1-V_6)$	Rel. Synaptic Current $(\text{Rel } E) \times (1-V_6)$
.07	.9663	.1783	.8217	.794
.09	.99966	.2162	.7838	.784
.11	.9831	.243	.757	.744
.05	.8578	.1281	.8719	.748
.06	.9234	.1548	.8452	.780
.08	.9906	.1988	(.8012)	≈.794

{here driving pot.
{compensates for less than
peak E

at T = .03 ⑯ = 5.88281
⑰ = 2.74438

net = 3.13843 slightly less than at .04
& right

1/7/66 checked same picture with 661.164

661.164 Slow E trans in ⑥ ~~&~~ monitor currents

Here cpt. ⑱ does not go neg. which fits the idea That in 661.144, this was due to pert. being on the near side of midpoint; here it is on the far side.

		Δ
.30	.05538	.00631
.28	.04907	.00652
.26	.04255	.00660
.24	.03595	.00654
.22	.02941	.00629
.20	.02312	

peak in ① occurs at T = .62

half max at T = .28

max slope is near at .25

whereas peak in ⑱ is at T = .26, which agrees quite well

---

peak in ⑥ occurs at T = .19

half peak occurs at about .06

max slope occurs a little earlier between .03 & .04

now peak E occurs at .092

peak ⑯ " " .07

} See left
because driving pot greater

But ⑯ - ⑰ must be looked at

at T = .07 ⑯ = 7.83028
⑰ = 5.63196
net = 2.19832

at T = .04 ⑯ = 6.80084
⑰ = 3.74664
net = 3.15420

Bob Burke gave me these figures 12/22/65 on yellow sheet

for MG & FDL summation.

MG alone (slow epsp)
- ampl 1.2 mV
- time to peak 2.95 msec
- mV/msec (20 to 80%) 0.75
- mV/msec/mV 0.80

$v \approx .017$

$t/\tau = .6$

FDL alone (fast epsp)
- ampl 1.55 mV
- time to peak 1.07 msec
- mV/msec (20 to 80%) 2.1
- mV/msec/mV 2.08 ?

$v \approx .022$

$t/\tau = .2$

Combined
- ampl 2.26
- time to peak 1.10 msec
- mV/msec ?
- mV/msec/mV

He found some non-linear loss
But when fast one was made a little later, added much better.

Here in ⑥ 20 to 80% slope

$$\begin{array}{r} V \\ .021967 \\ .009229 \\ \hline .012738 \end{array} \qquad \begin{array}{r} T \\ .16 \\ .08 \\ \hline .08 \end{array}$$

$$\text{slope} = .16 \times \frac{70}{4} = 2.8 \text{ mV/msec}$$

about 33% high

ampl in ⑥ was 18% high

Try $\varepsilon = .85$ in ②

1/7/66

662.002 Three Chain epsp sums
fast TRNS

Epeak = 1.0 in ② & ⑦
5.0 in ⑤ & ⑮

⑳ sums ⑥ + ⑪ ~~& comp~~ subtracts ①

for 70mV E_2

1.82
peak in ⑥ is .026 at T=.24 for E in 2nd cpt only

2.07
peak in ⑪ is .0296 at T=.84 for E in 5th cpt. only

3.0
peak in ① is .04286 at T=.68 for E in both places

⑳ is everywhere positive, max ≈ 4.8×10^{-5}
But between 3×10^{-5} & this for T=.24
to T=1.1

This implies departure from linearity ≈ 0.1%

	at T=.24	.68	.84
⑥	.0259734	.0146711	.0116785
⑪	.0045734	.0282284	.0296043
sum	.0305468	.0428995	.0412828
①	.0305140	.0428578	.0412458
diff	.0000328	.0000417	.0000370
⑳	.00003284	.00004176	.00003699

1/7/66 put in 1/10/66

662.003	Evalues .85 & 2.9	Kappas 70.
661.121	Monitor Current with E in ②	
546.101	fast 5 cps post	
556.101	slow " " "	
661.551	monitor J current	

664.141	$\Delta T = .10$	$\lambda_{0,13} = 8.$
664.142	.25	4.
664.143	.50	2.

not fits, first seek max T

1/7/66 midafternoon

measure 645.1 series
cf. p. 2, 16, 24

Things to do – write Marmon
Walter Freeman
? Brookhart & Katz.

Start outlining & writing this simulation summary

Further calculations

A. Monitor current with fast transient

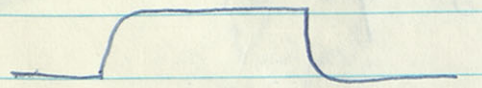
B. add uniform G – { slow trans to 556 ✓
& fit. { fast trans to 546 ✓

C. Then check go distortion ala 656 & 646

D. Test linearity for small perts. look for rule.

E. Test effect of varying duration of Square E ✓
TRNS E

F. Monitor current for a J (50%) ✓
or a large E (50%)



664.14 series using opt. 4 pert. of this kind.

31

13
14

Initially, $A = 1.0$
$B = 0$
and $\lambda_{B,A} = 50.$

E follows B

at Time change

Set $\lambda_{B,A} = 0$
$\lambda_{0,B} = 50.$

E follows B.

655.1 slow TRNS E   peak E ranges from 1.75 in ① to 33.64 in ⑩   17.1 in ⑧

pert V peak   .10   .73   .43

Here, time to peak, etc all increase monotonically with distance.

slopes — — all decrease " " " " "

Appropriate product (slope × time from 10% to peak) approx const.

Comparing 655.1 with 654.1

blunt   * in ① square E rel. low because duration long rel. to amplitude

sharp   in ⑩ " " rel. high " " short " " "

for the same reason square E in near pts gives rel. ~~S~~ smaller rising slopes

in far pts " " " larger " "

falling slopes very similar for pert at ③ or farther out.

∴ Best to prepare chart or graph from 655.1 & possibly only discuss comparison with square

*? Possibly chart only for Short Chain

? graph for long chain.

Now compare 655.1 slow TRNS } series

645.1 fast TRNS }

go to p. 56

1/9/66 (10)

Plans for paper on computations. Refer back to p. 8, 6,7 Titles, (6 joint) (20 joint), 30.

Point of departure for present series & this paper, is to ~~fix~~ fix epsp amplitude, and compare other features. Also, fix E time course.

Thus, we have ampl. = 0.10, 0.20, -0.05
we have ~~time course~~, square, slow TRNS, fast TRNS, finally varied

Strategy of presentation ① first, how much do we have to increase E as we go out?
② " " does this increase peak V " " " " ?
③ What does this do to shape, time of peak, etc.
④ How can one try to work backwards?
Problem of E time course versus location.
i.e. easy to work backwards if one or the other is given

Now, plan to go over the charts to note down here the points that need to be brought out in paper. It may prove to be wiser not to present square first.

654.1 square E value ranges from 1.265 in ① to 58.86 in ⑩ 18.5 in ⑧
very roughly approximates 1, 2, 3, 4, near in, but then sails off.
V peak ranges from .10 to .88 in ⑩ .55 in ⑧
Time to peak & slopes somewhat artefactual for pert in ①

654.2 E 2.76 in ① to 300 in ⑧
V in pert. .20 .965

654.5 g 9.9 in ① to 79.2 in ④

Square
However, neglecting artefactual complication of pert in ①
time from 10% to 90% to peak ≈ .19 for pts 1, 2, 3 ; ≈ .4 for cpt ⑩
time from rising to falling half max ≈ .43 for ② 1.45 for ⑩
time from 10% pt. to max .23 for ② .63 for ⑩
slope at rising half max (.1 series) .415 .24 for ⑩

Compare 646.130 see p. 22 & p. 12

→ get 3.54% peak distort at ① for $\varepsilon = 9.52$ in ③
at $T = .42$

This is 36% of the 9.84% value for pert in ①
which agrees well with p. 12 showing that at $T \equiv 1.0$ of step
value in ③ is 37% of value in ①

Here, this 2.95% value presumably corresp to $\approx \left(\frac{.049}{.163}\right)(9.8) \simeq 2.95$ ✓
QED

i.e. get same answer as with steps, if use peak distort, obtained when timing is for peak input. cpt. & then Δ in ① is compared with max amplitude in ①. ←

663.031 on p. 38 had unfavorable timing

54

1/9/66 (10 written above 9) Got back 663.032 and 645.100

663.032 Short Chain pair sinusoidal with perturbation.
compare with 663.031 (p.38) have begun with I.C from T=8.0 on p.38

	Steady State Values (integer even T.)		%	extremum	
1&6	.10968	≈ .1097	100	−.16288	9.25
2&7	.27880	≈ .2788	54.8	.08931	9.40
3&8	−.006807	≈ −.00681	30.1	.04906	8.55
4&9	−.018157	≈ −.01816	18.2	.029715	8.70
5&9	−.02058	−.02058	14.3	.023335	8.80
	agree well with (p.38)		see p.12, p.38	agrees with (p.38)	

starting T=8.5

cpt ⑪ gives ⑥ (control) − ① (distorted)

positive for all T

peak = .00480 at T=8.90

when value in ⑥ is −.0670
① is −.0718

i.e. distorted value is more neg. (less pos.) than control by 6.85%

distortion peak in ① is 2.95% of extremum in ⑥ which agrees with anticipations, see left

This time is .40 after pert. onset which agrees with epsp peak in ① for pert in ③ of 5.

cpt ⑫ gives ⑧ (control) − ③ (pert.)

positive for all T

peak = .016346 at T=8.60

when value in ⑧ is .04832
③ is .03197
.01635

distorted ~~value~~ is less pos. than control by 34%

This time is .10 after pert onset which agrees with epsp pert

Also, These approaches avoid true zero

It is interesting that fast + slow TRNS both give ~.15 as prod. of $\frac{dV}{dt}$ hlf/max and the time from 10% to max. This corresp. to p. 164 of Book 7. Also, with square E, get same answer for pert beyond ⑤, but for pert closer, get smaller product, meaning slopes abnormally low rel. to peak amplitude because of artefactual shape. ←

1/$\overset{10}{9}$/66

645.100 B or also named 661.101

fast TRNS

Single compartment, Found Epeak = 1.152
Cump
gives epsp peak = .10
at T = .20

refers back to p. 40

Also, here, initial Epeak of 2.0 gave epsp peak = .1665
at T = .20

④ Epeak occurs at T = .04
⑥ synaptic current peaks at T = .04

Now, need to measure these characteristics to tabulate with rest of 645.1 series

Now compare 645.1 & 655.1 long chain series.

slow trans T* = .092 larger area : Epeak range 1.75 in ① to 33.64 in ⑩
fast trans T* = .04 smaller area : 2.74 in ① 234. in ⑩

The farther out one goes, the more difference the area makes

for example for slow trans, Vpeak in ② is .106 ; in ⑥ is .279 ; in ⑧ is .426 ; in ⑩ .73
fast .112 .405 .602 ; .94

slow $\frac{dV}{dT}$ for ① .764 ④ .431 ⑩ .202
fast 1.63 more than double .677 .236 only about 17% increase

In other words, the fast transient makes much more difference to rise rate for near part than for far part. In fact, ① in short chain did not give quite a factor of two.

* There is a kind of shape invariance, taken from 10% point to 90% or peak & even to falling half max, shown by products of $\frac{dV}{dt}$ at half max, against time

Values of ④

664.141	664.142	664.143	T
.0144	.00724		.01
.0425	.0215		.02
.0721	.0369		.03

← ~factor 2

(1/11/66)

setup 664.411 fit
664.421 fit
664.430 prelim

Plan to modify – see p.64

Discrepancies due to fact the last T value before time change was not correct. Suspect program error as well; Marg was recently changing this part of the program.

best due →
TC of .23
finally was a

1/11/66 just got back the runs listed on p. 49

First look at 664.14 series of varied durations in ④

$\lambda_{15,14} = 50.$

664.141 with  $\Delta T = 0.10$, ε peak set at 8.0

cpt. ⑮ reached

.918 by	T = .05
.9817	.08
.9933	.10
.60	.11
.0815	.15
.0182	.18
.00669	.20
.00055	.25

cpt. ④ naturally (.20) peaked at T = .10 which was end of step.

cpt ① peaked .0752 at T = .26

664.142 $\Delta T = .25$, ε peak set at 4.0

? ⑮ off does not agree with previous

④ peaks .173 at T = .25, which is end of step.

① peaked .09154 at T = .35

664.143 $\Delta T = .50$, ε peak set at 2.0

⑮ off is extreme.

④ peaks .1284 at T = .50, which is end of step

① peaked .07684 at T = .50 " ?

Somehow ⑮ is not continuing correctly.

also ④ changes abruptly at .51

1/11/66

662.003 Three chain epsp sums

Kappa = 70 mV ✓

$\mathcal{E} = .85$ in 2 & 7

$\mathcal{E} = 2.9$ in 5 & 15

mV ✓

cf. p. 47

peak in ① is 2.13 at T = .60
⑥ 1.55 .24
⑪ 1.3 .84

Δ cf ⑳ $\approx .176 \times 10^{-2}$ mV ✓

departure from linearity $\approx$ 0.1 %

661.121 Monitor Current for $\mathcal{E}^{2.05}$ in ②

peak in ① is .100 at T = .28
② .10607 .24
Synaptic current ⑯ 2.335 .09
loss current ⑰ 1.743 .11
current from ② to ①; ⑱ .6867 .08
goes from + to − .36
neg peak −.06054 .52

This is because ② falls faster than ① remains neg.

* Kappas were incorrect

Expect max slope in ① at T = .08 because of ⑱ ✓ $\frac{.013}{.02}$

refer back to page 43-46

(1/11/66)

current step ↓
I. C. for T=1.

Setup 656.101 being 556.101 with current step
646.101 " 546.101 " " "

662.004 near apogee shifted in time

1/11/66

661.551 J current monitor J=250. in ⑤
time ran out at T=.52, need more time factor,
did not reach max; min in ①

max in ⑤ was −.092555 at T=.14
but very close much sooner.
i.e. flat top & later

⑯ max synaptic current occurs at T=.02
because driving pot falls too low later.

⑰ loss current peaks at T=.03
⑱ current from ② to ① is neg peak −.191
& remains neg. at T=.16

556.101 Short Chain, Slow TRNS, all cpts perturbed.
initial E=.5 peak gives .0873 in ① at T=.37

found E=.5787 gives .100225 at T=.37

546.101 Short Chain, Fast TRNS, all cpts perturbed.
initial E=1.0 gives .08746 at T=.20

found E=1.152 gives .100012 at T=.20

Strange that there is nearly factor of two between the two E values found.

1/12/-1/13/66

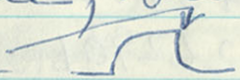
Computer down at NBS - also gibberish output.

Writing Mannen & Katz

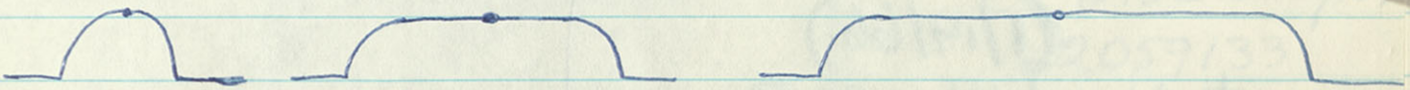
To library Reading Katz, Hebb, Young in Proc Roy Soc B 1965

Asked about "the Brain Research", "the Exp Brain Research", "Studies in Physiol." at library

refer back to pp 50 & 58

* Should modify 664 series, not only to avoid the incorrect T.C. time value, but also to avoid the sharp cut off 

This can be done as follows:



set $\lambda_{15,14}$ = ~~25.~~ 50. for 1st half ~~of~~ ΔT desired

Then, using T.C., set this equal to −50.

or possibly +25. & then −25.

Try out with one of these first.

If this works, perhaps do

T.C. at .05, .10, .20, .40

perhaps first in cpt. ②

St.st. Distortion figures

Slow 56	Fast 46
ε = 1.046 in ①	ε = 1.75 in ①
stst 26.4%	37.5%
ε = 2.109 in ②	ε = 4.255 in ②
	32.4%
ε = .578 in all	ε = 1.152 in all
26.4% in ①	40% in ①

older
656.111 St.st. with ε = 1.0456 in ①

① .2527586
② .1754855
③ .1262901
④ .09730108
⑤ .08388024

(1/14/66)
put in 646.101 B
656.101 B
646.150

See p. 70

Note that these steady state distortions are ~~greater~~ approx same than for larger pert in ① only. Why?, presumably because matching transient epsp peak at ~~.07~~ 0.1

66

1/14/66

Got back 646.101, 656.101; also 662.004 had too many param. needs to be reduced to 2 chains

646.101 Short chain, fast TRNS, with current Step.
ε peak = 0.578 in all fore cpts.

Got ε values here
interchanged by control

st. st.
~~con~~ control
here

~~distortion~~ do
trans. at T = .20
control
here

I.C. in ⑩ was neglected

Control		should be slow ε = 0.578 in all cpts.	should be fast ε = 1.152 in all cpts.
.3435548	①	.2528959	.2059133
.2385236	②	.1567471	.1168134
.1716561	③	.1001737	.0679347
.1322537	④	.0688922	.0424473
.1140118	⑤	.05500465	.0315753
	The extra sub. ⑥	.6337 ✓	~~.0464684~~

from cpts 11—15 st. st.
of earlier 646 runs

656.101

By mistake, I.C. in 10 was zero
I.C. in 9 was one

In cpt. 1 646.

St. st. ~~dist~~ distor in Cpt. ①

control .3436
.2529
Δ = .0907

656

control .3436
.2059
Δ = .1377

slow 26.4%

fast 40%

Remarkable coincidence, this agrees with ε = 1.0456 in ① only

1/14/66 664.4 series still —  — put in several days ago to run on older SAAM Tape

664.421 has T.C. at T=.25
monitor cpt. ⑮ looks O.K.
compare with 664.142 on page 58
Here, with $\varepsilon_{peak} = 4.$ cpt ① peaks .09154 at T=.37
for $\varepsilon = 4.57$ gives .10275 at T=.37

664.411 has T.C. at T=.10
Someone dropped card giving $\lambda_{015} = 50.$ after T.C.

664.143, someone got cards out of order.

Spent some time talking with Jose & being briefed somewhat on Kantorovich's proof of the convergence conditions for Newton's method. A reference is provided by the Pergamon Press translation

"Functional Analysis in Normed Spaces"

L.V. Kantorovich & G.P. Akilov
(Lenningrad Univ.)

slow

.28
.286549
.265763
.021386
7.46%

TRNS

Note that peak distort does not coincide with epsp peak

.20	.30	.32	.34
.281482	.287742	.288906	.290044
.262495	.266217	.267375	.268617
.018987	.021525	.021531	.021427
6.75%	7.48%	7.46%	7.4%

---

fast

T= .10	.14	.16	.15	.20
.274407	.277344	.278757	.278055	.281482
.254370	.254862	.256038	.255395	.259326
.020037	.022482	.022715	.023660	.022156
	8.1%	8.16%	8.5%	

1/17/66 New week. Try again to write in morning & leave computations, letters and chores to afternoon. also library research.

Received this morning, letters from Attinger (NATO Conference not definite until Jan 20)
& from Ainsley who says that C fiber λ is not available
Sending memo to K. Franks to setup seminar
Mon. March 21

Susa gave me a xerox copy of Jose's notes for the NIH Math. Tutorial that has been going on for past several weeks. Better look over before next one, ~~tomorrow~~.

646.101 B & 656.101B refer back to p. 66

656.101B Short Chain, Slow TRNS, Current Step.
26.4% steady state ε peak = .578 in all five cpts.

	at T = .36	.38	.35
control	.291156	.292242	.290603
here	.269924	.271279	.269264
	Δ = .021232	.020963	.021339
			7.35%
TRNS	7.3%	7.16%	

7.5% at T = .30

Compared with 9.76% for ε^{peak} = 1.0456 in ① alone
5.96 2.1086 in ② alone etc

646.101B Short Chain, fast TRNS, Current Step
ε peak = 1.152 in all five cpts.

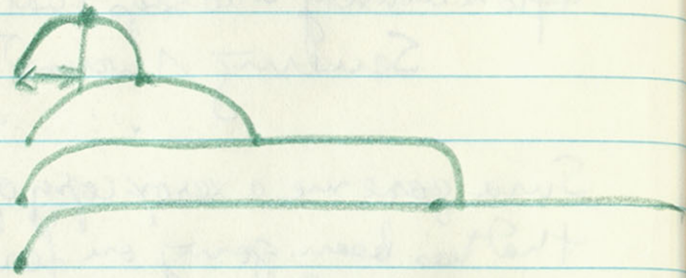
	control		
T = .20	.281482	T = .18	.280137
	.259326		.257572
	.022156		.022565
			8.06%

8.5% at T = .15

1/17/66 late

prd'n

664.412	$\Delta T = .05$
.422	.10
.432	.20
.442	.40



with $\lambda_{15,14} = -5a.$ after T.C.

1/17/66

646.150 Three chains, for TRNS, Curved Step.

$\mathcal{E} = 44.6$ in ⑤

Stst. control .3435548

here .3080370

.0355178

Stst. 10.36%

g.18 peaks at .101883 at T = .85

~~[illegible]~~ cf. ⑪ is 20 × Δ

⑪ .311904 at T = .85

⑰ .306810

Δ = .005094

1.63%

also .10174 at T = .80

.310255

⑰ .305168

Δ = .005087

1.64%

In between, surely rise to 1.65%

Say at T = .81 or .82

We also got into discussion of weak solutions & functional analysis as approaches to solutions which may satisfy the needs of our problem, but not the requirements of the idealized version of the problem when stated in terms of differential equations.

My approach to this was that when I go from continuous dendrites to compartmental dendrites, I am content to switch my focus from the one physical system to the other & not bother to try to prove that the solution for cpts. would converge to other soln.

Jose's comment was that it was after Newton & Leibniz that analysis became so highly developed in terms of idealized continuity; prior to that time the discrete approach was coequal to the continuous. In recent times, pendulum is swinging back. They key point is that our data & our interest may be nowhere near the infinite resolution implied by continuity. It may be much more realistic to define key quantities as integrals over a region in space & time. Such integral quantities can be handled by functional analysis & restrictions of idealized continuity can be avoided; then convergence of solutions can be obtained under these less stringent conditions, ~~which~~ in another approach, Sobolev treats weak solutions of diff. eqn as limits of approx solutions $L(u_j) = \epsilon_j$
If sequence of approx solns, u_j, produces sequence of small residual errors, ϵ_j, and if $\epsilon_j \longrightarrow 0$, then limit of u_j is a weak solution, even though it ~~is not~~ may not be a strict soln of $L(u) = 0$

1/18/65

Spend much of day with Jose & considering mathematical questions. Lecture was related to Chapter 3 of Pontryagin's book "Ordinary Differential Equations" Addison Wesley 1962

Question of uniqueness & equivalence classes.

If $\underset{\substack{\uparrow \\ \text{matrix}}}{\Phi} = (\underset{\uparrow}{\varphi_1}, \underset{\uparrow}{\varphi_2}, \underset{\uparrow}{\varphi_3} \cdots \varphi_n)$ is a fundamental

each a vector

Solution of a linear homogeneous system, Then there exist constant matrices, C, such that

$$\Psi = \Phi C$$

is also a fundamental solution.

This, I commented, means non-uniqueness; ~~that~~ José replied ~~that~~ yes, but that if we focus on the invariant aspects, we note that all of these solutions have the same eigenvalues, and they can be regarded as an "equivalence class". He emphasized that every real number corresponds to an equivalence class composed of corresponding objects that can be obtained as roots of various equations and as limits of various sequences. Returning to the fundamental solutions, the canonical form is then the Jordan canonical form which puts the eigenvalues on the main diagonal & handles off diagonal according to multiplicity of roots (see, e.g. final chapter of Pontryagin).

In particular, the questions of convergence touched on in those pages can be illustrated by ~~a solution~~ successive approximations to a solution:

(a) if we require very high spatio-temporal resolution, convergence may fail because of wild oscillations that are wilder, the higher the resolution requirement.

(b) for a coarser grained resolution, which may still be perfectly realistic in terms of operationally measureable quantities, convergence may be perfectly satisfactory.

1/19/66

Jose's comments on previous page were very interesting to me, because those mathematical devices for escaping the stringent conditions of idealized continuity found in differential equations — which are proving to be powerful new mathematical methods — are at least intuitively partly equivalent to my approach of replacing an idealized continuous physical model by a cruder compartmental physical model. Certainly, in biological & physical problems this is often very appropriate. It is relevant to consider what ~~the realistic~~ level of spatio-temporal resolution ~~irrelevant~~ ~~of the problem~~ is appropriate to any given problem. This is highly relevant to theoretical neurophysiology & perhaps I should consider more explicit further pursuit of this.

Jose did comment that these newer mathematical approaches — functional analysis on one hand, Sobolievs weak solutions on other, may spoil the hope of mathematical unification. I commented that Bohr's complementarity principle relates to this (I really should reread Bohr on this, because he did regard it as very basic to all Science). Jose also said that perhaps some further math - theory would develop for which all of these approaches become special cases. To some extent, it seems to me that one gets into questions of orientation & broadening of definitions, as for example classical physics → relativity. Here again, concept of equivalence classes may provide a way.

Thus, we could have d_0, data observed

d_1, simulated by model #1

d_j, " " " #j

However, point also came up that experimental data themselves are not directly related to "real system", but to some sort of a model of this system, this model being strongly influenced by the experimental procedures.

Here, we have to consider "operational definitions" of data variables.

Theory, according to Bridgeman, should be concerned with operational variables. Real point here is that it is only with the operational variables that one can test the adequacy of the correspondence between the theory domain and the experimental domain. Without a suitable expt., one cannot really test the correspondence of a more primitive theoretical variable with something corresponding to it in the real domain. If this primitive theoretical variable leads to sufficient testable predictions, it acquires an aura of reality. It may be very powerful & useful. As in physics, it may remain unobservable, or new expts may get closer to it.

1/19/66

Spent part of day checking into NATO Advanced Study Inst. plans & also, inquiry about program of Boulder summer conference.

* * *

1/20/66

Recall discussions with Moses about his paper on information ~~content~~ value of data. I was most concerned about consistency in the use of the word model. He sometimes uses the single word for three different meanings. These three kinds, he has sometimes distinguished in his seminars as follows:

general model { Number of cpts. specified
{ all x_{ij} unspecified

particular model { number of cpts specified
{ some $x_{ij} = 0$
{ other x_{ij} ~~constrain~~ may be constrained to certain ranges of values

specific model { all x_{ij} values specified.
{ Used for specific simulations.

He likes to use model most for the last case. Then, I would propose that the first two should be called model domain, or something like this.

Also, sometimes he semantically confuses model with actual system. One should aim to be consistent about correspondences & distinctions here. "epistemic correlations" of ? Fulton ?. at Yale However see left.

setup 664. (1/20/66) mod.

664.413
.423
.433
.443

3 here means C version

1/20/66

Title for paper that should now be ground out.
refer back to p. 52 & pp. 7   new variant

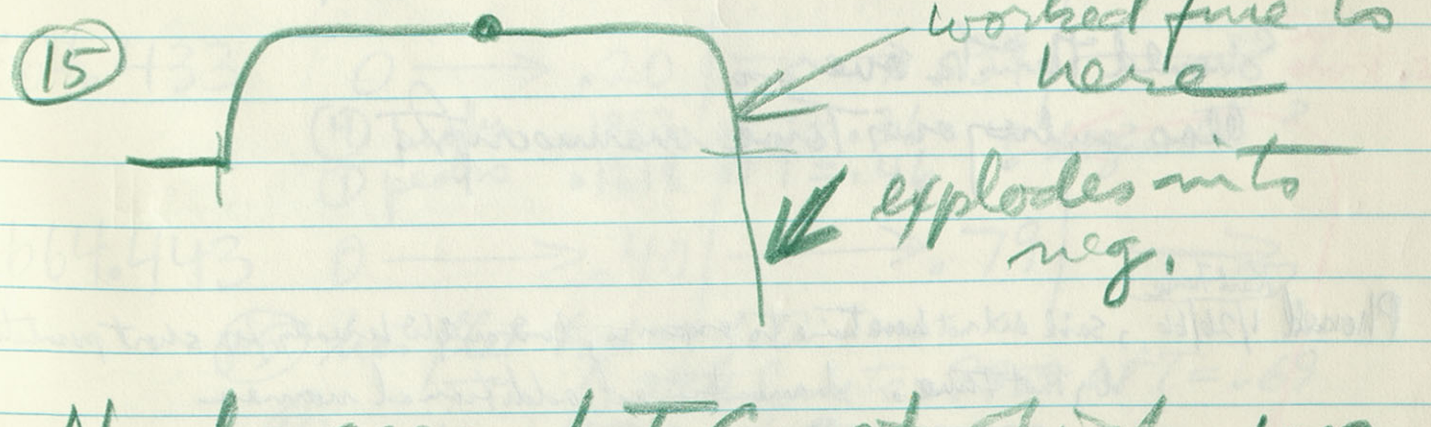
Distinguishing synaptic potentials computed for different { → locations of synaptic activity.
→ ~~spatial~~ distributions of synaptic conductance change

↑ actually, square & TRNS G imply temporal as well as spatial

---

664. Series refer back to p. 71 ~~&~~ 68

prepare C versions to correct for fact that ⑮ went neg. as soon as T = two original TC value



Need a second T.C. at which we set $\lambda_{0,13} = 0$.

64297

Karl Frank phoned and suggested a symposium on Math. Models for Neurophysiol Group on afternoon before Atlantic City - Fed Meetings 1st session

↑ i.e. Mon April 11 ↑ Tues April 12

He & Mike & Patton had in mind
Math Models of ~~Neurons~~ & Synapses

(.5)

He thought of Moore - 10 minute talk on modeling
but Moore not available

Also, they thought of including Don Wilson
Leon Harmon
Derek Fender
Fred Hiltz

(.6)

Thought of me as a chairman (organizer?)
&/or contributor.

Should think over.
Also sending over Towe manuscript.

Phoned (Karl Frank) 1/26/66, said did not have time to organize, but might be ready for short presentation by that time. I mentioned additional names

Belmont Farley } best
George Gerstein }
Ted Lewis good analogs & Harmon
Perkel temporal summation

1/21/66

Read Freeman's manuscript.

Afternoon, took Avo. Son to G. W. Hospital

1/24/66 Read Tone manuscript for K. Franks

roughed out memo.

Afternoon — Received 664.000 Series output

[illegible]

664.413 0 → 0.05 | → 0.09 | →

z_{013} = 25.

(15) peaks ~~at~~ .9179 at T = .05 get sym. above .05

(4) peaks .3822 T = .08

(1) peaks .1218 T = .23

664.423 0 → .10 | → .19 | →

(15) peaks .99326 at T = .10 get sym above .10

(4) peaks .2913 @ T = .17

(1) peaks .13414 .30

664.433 0 → .20 | → .39 | → Sym about .20

(4) peaks .1983 at T = .36 ? ~~diagnostic~~ ?

(1) peaks .1218 at T = .46

664.443 0 → .40 | → .79 | →

(15) has flat top = 1.0

starts down to .9959 at T = .69

(4) peaks .1502 at T = .75

(1) " .108998 T = .83

Mary fixed program

Got new run 2/7/66

The key to success may be to omit figures. This simplifies task, but may cost a lot in readability. But perhaps justified in getting over the hump.

1/25/66

Completed refereeing Towe manuscript & Freeman manuscript. I really must quite computing & all other things & concentrate on short papers. It is becoming urgent that I record at least the outline of the model I used in the Olfactory bulb computations & ~~even~~ in the earlier Ojai & Stockholm computations.

I Theory for computing spatio temporal ~~[illegible]~~ membrane potential disturbances ~~over~~ of ~~both active and~~ neurons having ~~regions of~~ both active and passive ~~[illegible]~~ membrane regions.

II Theory for computing extracellular neuronal potentials generated by ~~specified~~ given spatio temporal membrane potential disturbances.

these two

The purpose of this paper is provide a brief outline of the theoretical basis for computations that have been carried out over the past several years, and which have been only incompletely reported in the literature.

Also must write up

Distinguishing synaptic potentials computed for different spatio temporal distributions of synaptic conductance change.

also olfactory Bulb manuscript.

Must proceed to write these up briefly & use a basis for various invited talks.

1/26/66

Made a start on writing first several pages of paper I listed on p.84. Also looked over slides & prints for dendro-dendritic synaptic pathway talk to give to Biophysics Lab Seminar (Taylor, Chandler, etc)

1/27/66 Gave talk & had interested discussion.

Reviewed overall dendritic story

Then gave same set of slide prints as at Tokyo.

Chandler was interested in one dimensional aspect.

Ehrenpreis was interested in argument that axon provides less current.

It may be desirable to polish off the paper with Gordon very soon now, referring to computational ~~details~~ model to be presented more fully elsewhere.

1/28/66 Worked on manuscript. (I p.84)

1/31/ — 2/2/66 Heavy snow; worked at home on manuscript.

Attinger wrote that NATO Conference plans cancelled.

2/3/66 Continued manuscript & started writing

Also Phil Nelson phoned. We will get together next week on the series of 5 papers planned together. (See pp. 7, 52, 80)

2/3 & 2/4 Received dendrodendritic reprints sent 10 airmail to Gordon
25 reg. to Tom
25 —— Milton

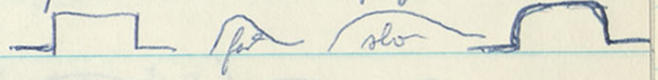
Worked on table of definitions for paper; this was second table (compartmental) and was given to Dorothy to type.

Also refereeing job & invitation from Windle to become an Assoc. Editor.

got back 664.433 now ran O.K. after Meg.
fixed test on T.C. final times by adding
an E. See p.82

2/7/66 New week, get back to paper for series with K, Phil + Bob
see pp 6 & 7, 52, 58-72 calcs, 80

Title for my short paper:
Distinguishing synaptic potentials computed for different spatio-temporal distributions of synaptic conductance changes.

Off the cuff, before reviewing earlier notes in this notebook, the points are:
① adjust ε peak, whatever spatio-temporal aspect, to give preassigned amplitude of $\overset{\text{ipsp}}{\text{epsp}}$ at soma
ⓐ (This task is uniquely suited to computation
ⓑ differs from emphasis in earlier papers.
② Time course choice 

③ Increase ε with distance out
④ rate of rise
time to peak } characteristics
rate of fall
⑤ Attempts to measure impedance change.
⑥ Linearity & Non-linearity
Nearly all of the computations do not provide for anomalous rectification.
⑦ Time course of ε, of synaptic currents, of V at site, of V at soma.
see p. 46

p. 20 Comments on joint paper.
p. 30 Summarizes most of the computation series.

This week went by quickly with two half days sick leave for head cold. Also wrote note to Attinger.
Friday 2/11/66 phoned J. B. Best. Also noticed J. B.'s article in Science.
See next page.

Red ink notes in folder. These notes were dated 4/27/65, and must correspond to p. 165 of book 6, but were not transcribed because of pressure of dendrodendritic story.

see p. 135 book 6

Non-Steady State, but passive

$$I_m R_m = V + \frac{\partial V}{\partial T}$$
$$= U - \varphi + \frac{\partial U}{\partial T} - \frac{\partial \varphi}{\partial T}$$

$\therefore$ PDE is $$\frac{\partial^2 U}{\partial Z^2} = U - \varphi + \frac{\partial U'}{\partial T} - \frac{\partial \varphi}{\partial T}$$

also go to page 92

For sinusoidal st. st. $$\frac{d^2 U}{d Z^2} = (1 + j\omega \cancel{\tau})(U - \varphi)$$

For non-passive as well as non steady state

$$I_m R_m = k^2 (U - U_s - \varphi) + \frac{\partial U}{\partial T} - \frac{\partial \varphi}{\partial T}$$

see N.Y. Acad.

let $W = U - U_s$

Then $$\frac{\partial^2 W}{\partial Z^2} = k^2 (W - \varphi) + \frac{\partial W}{\partial T} - \frac{\partial \varphi}{\partial T}$$

& for sinusoidal st st.

$$\frac{d^2 W}{d Z^2} = (k^2 + j\omega \cancel{\tau})(W - \varphi)$$

$\cosh Z \rightarrow \cosh \{\sqrt{1 + j\omega\tau}\, Z\}$

but $\sqrt{1 + j\omega\tau} = \sqrt{(r+1)/2} + j\sqrt{(r-1)/2} = a + jb$ see 1960 paper

$\therefore \cosh Z \longrightarrow \cosh \{aZ + jbZ\}$

$= \cosh aZ \cosh jbZ + \sinh aZ \sinh jbZ$

$= \cos bZ \cosh aZ + i \sin bZ \sinh aZ$

2/14/66 Best's article in Science – compare with mine.

Science Feb 11, 1966 Vol. 151, # 3711, p. 707–709 Best & Elshtain

Unconditioned response to electric shock: mechanism in planarians.

Abstract. Some implications of a math. theory relating neuronal geometry to the parameters of excitation in unconditioned response – – " . .

He deals with redist. of conc. of ions in closed cylinders.

Begins with $J = -D\,dC/dx + Dq\,EC/RT$

J is flux of ions, D diff coeff, E = field intensity, charge q per mole.

Theory apparently presented in worm runners digest Jan 1966

perturbation at extremity of cylinder depends upon half length, L.

For monophasic square wave, E by t, they get threshold condition

$$1 \leq (EL/\lambda)[1 - \exp(-2Dt/L^2)$$

where λ is rheobasic potential.

∴ for half length, L, rheobasic E is $E_r = \lambda/L$

From my point of view, this use of E_r and λ is unfortunate.

chronaxie $t_c = (L^2/2D)\ln 2$

cylinders
long neurons have low E_r and long t_c
short " " high E_r & short t_c

but he does not quantify length as I do in terms of Z length.

Now, look back to my pp 117–165 of book 6
4/8/65 – 4/29/65 which produced
a ditto manuscript of 13 pages and 37 equations.

This manuscript dealt with "Steady Electric Field", but red-ink notes (see p. at left) began extension to transients. Consider this further now, because of relevance to Best's work.

See previous two pages

2/14/66 passive membrane, non-steady state PDE

$$\frac{\partial^2 U}{\partial Z^2} = U - \varphi + \frac{\partial}{\partial T}(U - \varphi)$$

where $V_e = V_{e0} + \varphi(Z)$

reference point, a constant

$$U = V + \varphi$$
$$= V_i - V_e - E_r + \varphi$$
$$= V_i \underbrace{- V_{e0} - E_r}_{\text{constant}}$$

$$\therefore \frac{\partial U}{\partial Z} = \frac{\partial V_i}{\partial Z} \quad \text{and} \quad \frac{\partial U}{\partial T} = \frac{\partial V_i}{\partial T}$$

Consider step, $\varphi(\cancel{Z})$ applied at $T = 0$

Then $\frac{\partial \varphi}{\partial T} = 0$ and $U(Z,0) = V(Z,0) + \varphi(Z$

& we assume $V(Z,0) = 0$, $\therefore U(Z,0) = \varphi(Z)$

Problem becomes $\frac{\partial^2 U}{\partial Z^2} = U - \varphi + \frac{\partial U}{\partial T}$

Take $U(Z,\infty)$ from steady state solution

~~Define~~ Then $\frac{\partial^2 U}{\partial Z^2} = U(Z,\infty) - \varphi$ at $T = \infty$

Define $Y(Z,T) = U(Z,T) - U(Z,\infty)$

giving $Y(Z,0) = \varphi(Z) - U(Z,\infty)$
$= -V(Z,\infty) =$

and $Y(Z,\infty) = 0$

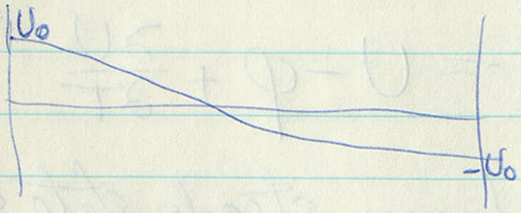
93

note $\tanh(\frac{1}{2}Z_m) = \frac{\cosh Z_m - 1}{\sinh Z_m}$

$= \frac{\sinh Z_m}{\cosh Z_m + 1}$

See Dwight p. 144

This $V(Z,\infty) =$



$U_0 = b\tanh(\frac{1}{2}Z_m)$

in general $U(Z,\infty) = U_0\cosh Z - \varphi^*\sinh Z$

for $\varphi = bZ$ (see eq 21) $U(Z,\infty) = U_0\cosh Z - b\sinh Z + bZ$

$= b\tanh(\frac{1}{2}Z_m)\cosh Z - b\sinh Z + bZ$

But $V(Z,\infty) = U - \varphi =$

$-V(Z,\infty) = b\sinh Z - b\tanh(\frac{1}{2}Z_m)\cosh Z$

2/14/66 Now the BVP simplifies to

$$\frac{\partial^2 Y}{\partial Z^2} = Y + \frac{\partial Y}{\partial T}$$

with $\frac{\partial Y}{\partial Z} = 0$ at $Z = 0$ & Z_m

& with $Y(Z,0) = -V(Z,\infty)$

$Y(Z,\infty) = 0$ which makes it seperable.

Compare N.Y. Academy paper.

Here $$Y(Z,T) = \sum_{n=0}^{\infty} C_n \cos(n\pi Z/Z_m) e^{-\alpha_n^2 T}$$

where $\alpha_n^2 = k^2 + (n\pi/L)^2$

and $$C_n = \frac{\int_0^{Z_m} (-V(Z,\infty)) \cos(n\pi Z/Z_m) dZ}{\int_0^{Z_m} \cos^2(n\pi Z/Z_m) dZ} \quad = \frac{Z_m}{2} \text{ for } n>0$$

here $k^2 = 1$, and for const field $\phi = bZ$

eq. (23) of manuscript gives $V(Z,\infty) = \frac{b \sinh(\frac{1}{2}Z_m - Z)}{\cosh(\frac{1}{2}Z_m)}$

or $\boxed{b \tanh(\frac{1}{2}Z_m) - bZ}$

Symmetry at left means that for ~~odd~~ even values of n, $C_n = 0$

$$C_0 = \frac{b}{Z_m}\int_0^{Z_m} \sinh Z\, dZ - \frac{b \tanh(\frac{1}{2}Z_m)}{Z_m}\int_0^{Z_m} \cosh Z\, dZ$$

$$= \frac{b}{Z_m}(\cosh Z_m - 1) - \frac{b\tanh(\frac{1}{2}Z_m)}{Z_m}(\sinh Z_m)$$

which equals zero, because (see upper left identity) of symmetry.

$$\int e^{ax} \sin px \, dx = \frac{e^{ax}(a \sin px - p \cos px)}{a^2 + p^2}$$

$$\boxed{\int e^{ax} \cos px \, dx = \frac{e^{ax}(a \cos px + p \sin px)}{a^2+p^2}}$$

$$\sinh ax \cos px = \frac{e^{ax} - e^{-ax}}{2} \cos px$$

$$\therefore \int \sinh ax \cos px \, dx = \frac{a \cosh ax \cos px + p \sinh ax \sin px}{a^2+p^2}$$

$$\cosh ax \cos px = \frac{e^{ax} + e^{-ax}}{2} \cos px$$

$$\therefore \int \cosh ax \cos px = \frac{a \sinh ax \cos px + p \cosh ax \sin px}{a^2+p^2}$$

2/14/66 for $n = 1$

$$C_1 = \frac{2b}{Z_m}\int_0^{Z_m} \sinh Z \cos(\pi Z/Z_m)\, dZ - \frac{2b \tanh\left(\frac{Z_m}{2}\right)}{Z_m}\int_0^{Z_m} \cosh Z \cos(\pi Z/Z_m)\, dZ$$

$$= \frac{2b}{Z_m}\left[\frac{\cosh Z \cos\left(\pi \frac{Z}{Z_m}\right) + \frac{\pi}{Z_m}\sinh Z \sin\left(\pi \frac{Z}{Z_m}\right)}{1+\left(\frac{\pi}{Z_m}\right)^2}\right]_0^{Z_m}$$

$$- \frac{2b \tanh\left(\frac{Z_m}{2}\right)}{Z_m}\left[\frac{\sinh Z \cos\left(\pi \frac{Z}{Z_m}\right) + \frac{\pi}{Z_m}\cosh Z \sin\left(\pi \frac{Z}{Z_m}\right)}{1+\left(\frac{\pi}{Z_m}\right)^2}\right]_0^{Z_m}$$

for $n = 2$ or any even integer, this term is $+1$

$$= \frac{2b}{Z_m}\left\{\frac{-\cosh Z_m \enclose{circle}{-1} + 0}{1+\left(\frac{\pi}{Z_m}\right)^2}\right\} - \frac{2b \tanh\left(\frac{Z_m}{2}\right)}{Z_m}\left\{\frac{-\sinh Z_m - 0 + 0}{1+\left(\frac{\pi}{Z_m}\right)^2}\right\}$$

see p 93

$$= \frac{2b}{Z_m\left(1+\left(\frac{\pi}{Z_m}\right)^2\right)}\left\{-\cosh Z_m - 1 + (\cosh Z_m - 1)\right\}$$

and get zero

$$= \frac{-4b}{Z_m\left(1+\left(\frac{\pi}{Z_m}\right)^2\right)}$$

for odd n

get $$\boxed{\frac{-4b}{Z_m\left(1+\left(\frac{n\pi}{Z_m}\right)^2\right)}}$$

97

$$\frac{ba^2}{s^2(s^2-a^2)} \rightarrow \frac{b}{a}\sinh at - bt$$

$$e^{j\omega t} = \cos\omega t + i\sin\omega t$$

$$e^{j\omega t + j\theta}$$ has phase shift θ

Laplace transform with respect to X.

for $\varphi(x)$

get $$s^2 f - sF_0 = (1+j\omega\cancel{\tau})\left(f - \frac{b}{s^2}\right) \qquad (f - L\{\varphi\})$$

$$f(s^2-1-j\omega\cancel{\tau}) = sF_0 - \frac{(1+j\omega\cancel{\tau})b}{s^2}$$

$$f = \frac{sF_0}{s^2-1-j\omega\cancel{\tau}} - \frac{(1+j\omega\cancel{\tau})b}{s^2(s^2-1-j\omega\cancel{\tau})} \qquad \frac{(1+j\omega\tau)L\{\varphi\}}{s^2-1-j\omega\tau}$$

$$F = F_0\cosh\sqrt{1+j\omega\cancel{\tau}}\,X - \frac{b\,\sinh\sqrt{1+j\omega\cancel{\tau}}\,X}{\sqrt{1+j\omega\tau}} + bX$$

see p. 102

$$\underbrace{~~= (F_0-1)\cosh\sqrt{1+j\omega\tau}\,X + 1~~}$$

$$\varphi * \left(\sqrt{1+j\omega\tau}\,\sinh\sqrt{1+j\omega\tau}\right.$$

$$= \frac{d\varphi}{dx} * \cosh\sqrt{1+j\omega\tau} - \varphi(x)$$

~~when $X=0$, $F = F_0 - 1 + 1 = F_0$~~

This cosh has already been worked out on p. 89

$$~~F(X) = (F_0-1)~~\{\cos\beta X\cosh\alpha X + i\sin\beta X\sinh\alpha X\} + 1$$

where $\alpha = \sqrt{(r+1)/2}$ and $r = \sqrt{1+\omega^2\cancel{\tau}^2}$

$\beta = \sqrt{(r-1)/2}$

Alternative

$$\cosh\{\alpha X + j\beta X\} = ~~\frac{e^{\alpha X}+e^{-\alpha X}}{2}~~ \frac{e^{\alpha X + j\beta X} + e^{-\alpha X - j\beta X}}{2}$$

See bottom p. 100

2/15/66 Received letter from Jordon with needed figure
Need to write J. B. Best very soon.
Also, before continuing from page 96, note back to p. 92 & p. 89

~~Suppose $\varphi(z)$~~ Seriously consider changing all Z to X, because Z is used for impedance & for complex quantities

external pot = $\varphi(x)e^{j\omega t}$

Suppose $\varphi(X\cancel{t}) = \underline{bXe}^{j\omega t}$

expect $U(X,t)$ to be $F(\cancel{X,t}\,(X))\cdot e^{j\omega t}$

↑ complex
may give different phase shift for different X

All this is implicit in the expression, p. 89, for sinusoidal st st,

$$\frac{d^2U}{dX^2} = (1+j\omega\cancel{\tau})(U - \varphi)$$

where U and φ are complex
with B.C. $\frac{dU}{dX} = 0$ at both ends.

If $U(X,t) = \underset{\text{complex}}{F(X)}\, e^{j\omega t}$

$(F(x) - \varphi(x))$ in general

Then $$\frac{d^2F}{dX^2} = (1+j\omega\tau)(\cancel{-bX} + F)$$

~~or $\frac{d^2F}{dX^2} - (1+j\omega\tau)F = -(bX + j\omega\tau)$~~

go to p. 97, 4 lines down

Found

dated 3/26/62

entitled "Summary of results obtained for Cole's problem of stability in sphere.

Also have carbon copy of memo to Cole dated 3/26/62.

$$|R_3| > \left\{ \frac{bR_i}{1} + \frac{bR_e}{2} \right\}$$ for n=1

$$\boxed{b < \frac{|R_3|}{\frac{1}{2}R_e + R_i}}$$

given this condition, should settle down

without this condition, should get explosion

st.st. Coeff of cosine term is zero for centrally located current electrode.

However not for off center.

If located midway along radius & if $|R_3|$ of order $2bR_i = 2bR_e$

then cosine coeff of order of uniform term.

Phoned him 4PM ~~3/26/62~~ 2/15/66

2/15/66 Mike Bennett just telephoned (11:20 AM) (Code 212 SW-5 3600)

See left.

He wanted to confirm a result he got from me thru K.S. Cole four years ago.

Had to do with voltage clamping sphere when there is a constant negative resistance.

The critical radius he got from Cole was $\frac{R_3}{\frac{1}{2}R_1 + R_2}$

where R_3 is R_m, R_1 is R_e, R_2 is R_i

He would like to know if this is correct, and also if I have proof that if it holds steady, it must be clamped to value that is constant everywhere.

Their current electrode is centered.
Their potential electrode is near surface.

Result from previous pages is that

$$F(X) = F_0 \cosh\sqrt{1+j\omega\cancel{\tau}}\,X + \underbrace{\phi(x) - \frac{d\phi}{dX}^{*} \cosh\sqrt{1+j\omega\cancel{\tau}}\,X}_{\text{or This part } = -\phi^{*}\left(\sqrt{1+j\omega\cancel{\tau}}\ \sinh\sqrt{1+j\omega\cancel{\tau}}\,X\right)}$$

Referred to evidence of Pat Wall
J. Physiol. 180 pp (116-133)

2/15/66 Belmont Farley telephoned (5:30 PM)

Hoped I would discuss evidence & implications of active vs passive dendrites.

I could survey dendrites in terms of what I already have. 1962 conclusion
Bulb conclusion
Dendro-dendritic

Consider simplifying expressions by letting

Small $\sqrt{z} = \sqrt{1+j\omega\tau} = \sqrt{r}e^{j\theta/2}$

$= \alpha + j\beta$

where $\alpha = \sqrt{(r+1)/2}$

$\beta = \sqrt{(r-1)/2}$

And see 1960 paper where $re^{j\theta} = 1 + j\omega\tau$

Now that plan to use X in place of Z

Could also use L for $X_m = Z_m$

Also $\omega \to 0$, $F_0 \to V_0$ of earlier ditto eq(22)

$\therefore$ also $F_0 = \frac{b}{\sqrt{1+j\omega\tau}} \tanh\left(\frac{X_m}{2}\sqrt{1+j\omega\tau}\right)$

~~Also $\frac{b}{\sqrt{1+j\omega\tau}}$ sinh $\left(\frac{X_m}{2}\sqrt{}\right)$~~

See # 653.5 on p. 144 of Dwight also in CRC math tables p. 432 of 12th ed.

late
2/16/66 Too many interruptions; redo p. 97

$$\varphi * a\sinh ax = \int_0^x \underbrace{\varphi(\tau)}_{u}\ \underbrace{a\sinh(ax-a\tau)\,d\tau}_{-dv}$$

$\int u\,dv = uv - \int v\,du$

by parts $$\overset{-}{=}\Big[\varphi(\tau)\cosh(ax-a\tau\Big]_0^x + \int_0^x \frac{d\varphi}{dx}\cosh(ax-a\tau)\,d\tau$$

$$= -\varphi(x) + \frac{d\varphi}{dx} * \cosh ax$$

$\uparrow$ note that $\varphi(0)=0$ has been used here

Now, when $\varphi = bx$

Then $$\varphi * a\sinh ax = -bx + b\left[\frac{\sinh(ax-a\tau)}{-a}\right]_0^x$$
$$= -bx + \frac{b}{a}\sinh ax$$

$\therefore$ with $\varphi = bx$ and $a = \sqrt{1+j\omega\tau}$

The result on p. 97 & bottom of p. 100 becomes

$$F(x) = F_0\cosh\sqrt{1+j\omega\tau}\,x + bx - \frac{b\sinh\sqrt{1+j\omega\tau}\,x}{\sqrt{1+j\omega\tau}}$$

Now $$\frac{dF}{dx} = F_0\sqrt{1+j\omega\tau}\sinh\sqrt{1+j\omega\tau}\,x + b - b\cosh\sqrt{1+j\omega\tau}\,x$$

for $x=0$, $\frac{dF}{dx} = 0 + b - b = 0$, as it should

next, get expression for F_0 that satisfies B.C. at x_m

$$\frac{dF}{dx} = 0 = F_0\sqrt{1+j\omega\tau}\sinh\sqrt{1+j\omega\tau}\,x_m + b - b\cosh\sqrt{1+j\omega\tau}\,x_m$$

$$\longrightarrow F_0 = \frac{b}{\sqrt{1+j\omega\tau}}\left(\frac{\cosh\sqrt{1+j\omega\tau}\,x_m - 1}{\sinh\sqrt{1+j\omega\tau}\,x_m}\right)$$

which may transform to a simpler form — yes see left

This should reduce to previous result as $\omega \to 0$

Also should seek the general expression for any $\varphi(x)$

from bottom of p. 104, get, when ~~using~~ mult. by complex conjugate above & below

$\sinh^2 - \cosh^2 = -1$

$$F_0 = \left[\frac{b(\alpha - j\beta)}{\alpha^2+\beta^2}\right]\left[\frac{\sinh\alpha L/2 \cosh\alpha L/2 \left(\sin^2\beta L/2 + \cos^2\beta L/2\right) + j\left(\sinh^2\alpha L/2 \sin\beta L/2 \cos\beta L/2 - \cosh^2 \sin\beta L/2 \cos\beta L/2\right)}{\sinh^2\alpha L/2 \sin^2\beta L/2 + \cosh^2\alpha L/2 \cos^2\beta L/2}\right]$$

~~#~~ make use of $\sinh x \cosh x = \frac{1}{2}\sinh 2x$

and $\sinh^2 x = \cosh^2 x - 1$

~~$\sinh^2 x \sinh^2 y = \cosh^2 x \cosh^2 y - \cosh^2 x - \cosh^2 y + 1$~~

$$F_0 = \left[\frac{b(\alpha - j\beta)}{\alpha^2+\beta^2}\right]\left[\frac{\frac{1}{2}\sinh\alpha L + \frac{1}{2} j \sin\beta L}{\cosh^2\alpha L/2 - \sin^2\beta L/2}\right]$$

$$= \left(\frac{b/2}{\alpha^2+\beta^2}\right)\left(\frac{\alpha\sinh\alpha L + \beta\sin\beta L - j(\beta\sinh\alpha L + \alpha\sin\beta L)}{\cancel{\sinh^2\alpha L/2 \sin^2\beta L/2 + \cosh^2\alpha L/2 \cos^2\beta L/2}\ \cosh^2\alpha L/2 - \sin^2\beta L/2}\right)$$

now, as $\omega \to 0$, $r \to 1$, $\theta \to 0$, $\beta \to 0$, $\alpha \to 1$

then above reduces to

$$F_0 = \left(\frac{b/2}{1}\right)\left(\frac{\sinh L + 0 - j(0+0)}{\cosh^2 L/2}\right)$$

$$= \left(\frac{b}{2}\right)\frac{\sinh L}{\frac{1}{2}(\cosh L + 1)}$$ from Dwight 652.6

$$= b\tanh(L/2)$$ Dwight 653.5

which agrees with eq (22) on p. 8 of early ditto

for denom, note that $\sin^2(y/2) = \frac{1}{2}(1 - \cos y)$

$\cosh^2(x/2) = \frac{1}{2}(\cosh x + 1)$ $\therefore$ denom $= \frac{1}{2}(\cosh\alpha L + \cos\beta L)$

2/16/66 5 P.M.

Worked hard today, writing Computed Synaptic Potentials manuscript

Now look at pp 101-102

In this paper, plan to replace $\bar{Z}$ with X
Z_m with L

Also note if $1+j\omega\tau = z = re^{j\theta}$ $\rightarrow$ with $r = \sqrt{1+\omega^2\tau^2}$ and $\tan\theta = \omega\tau$

Then $\sqrt{1+j\omega\tau} = \sqrt{z} = \sqrt{r}\,e^{j\theta/2}$

$= \alpha + j\beta$

where $\tan\frac{\theta}{2} = \sqrt{\frac{1-\cos\theta}{1+\cos\theta}}$

but $\cos\theta = \frac{1}{r}$

$\therefore \tan\frac{\theta}{2} = \sqrt{\frac{1-\frac{1}{r}}{1+\frac{1}{r}}}$ ~~$= \sqrt{\frac{r-1}{r+1}}$~~

$\sin\frac{\theta}{2} = \sqrt{(1-\frac{1}{r})/2}$

$\cos\frac{\theta}{2} = \sqrt{(1+\frac{1}{r})/2}$ ~~$= \sqrt{r}\sqrt{(r-1)/2}$~~

where

$\beta = \cancel{\alpha} = \sqrt{r}\sqrt{(1-\frac{1}{r})/2} = \sqrt{(r-1)/2}$

$\alpha\ \cancel{\beta} = \sqrt{r}\sqrt{(1+\frac{1}{r})/2} = \sqrt{(r+1)/2}$

Now, look at $F_0 = \frac{b}{\alpha+j\beta}\tanh\left(\frac{L}{2}(\alpha+j\beta)\right)$

$= \frac{b}{\alpha+j\beta}\left[\frac{e^{\frac{L}{2}(\alpha+j\beta)} - e^{-\frac{L}{2}(\alpha+j\beta)}}{e^{\frac{L}{2}(\alpha+j\beta)} + e^{-\frac{L}{2}(\alpha+j\beta)}}\right]$

Now $e^{\frac{L}{2}(\alpha+j\beta)} = \left(e^{\frac{\alpha L}{2}}\right)\left(e^{j\beta L/2}\right) = e^{\alpha L/2}\left\{\sin\left(\frac{\beta L}{2}\right) + j\cos\left(\frac{\beta L}{2}\right)\right\}$

$e^{-\frac{L}{2}(\alpha+j\beta)} = \left(e^{\frac{-\alpha L}{2}}\right)\left(e^{-j\beta L/2}\right) = e^{-\alpha L/2}\left\{-\sin\left(\frac{\beta L}{2}\right) + j\cos\left(\frac{\beta L}{2}\right)\right.$

$\therefore$ numerator of [ ] is $\left(e^{\alpha L/2} + e^{-\alpha L/2}\right)\sin\beta L/2 + \left(e^{\alpha L/2} - e^{-\alpha L/2}\right)j\cos\left(\frac{\beta L}{2}\right)$

$2\cosh\alpha L/2\,\sin\beta L/2 + j2\sinh\alpha L/2\,\cos\beta L/2$

denom is $2\sinh\alpha L/2\,\sin\beta L/2 + j2\cosh\alpha L/2\,\cos\beta L/2$

105

alternate approach to $\tanh(x+iy) = \dfrac{\tanh x + \tanh iy}{1 + \tanh x \tanh iy}$

$$= \frac{\tanh x + i \tan y}{1 + i \tanh x \tan y}$$

$1 + \tan^2 = \sec^2$

$$= \frac{\tanh x + \tanh x \tan^2 y + j (\tan y)\overbrace{(1 - \tanh^2 x)}^{\operatorname{sech}^2 x}}{1 + \tanh^2 x \tan^2 y}$$

$$= \frac{\tanh x \sec^2 y}{1 + \tanh^2 x \tan^2 y} + \frac{j \operatorname{sech}^2 x \tan y}{1 + \tanh^2 x \tan^2 y}$$

$$= \frac{\sinh x \cosh x}{\cosh^2 x \cos^2 y + \sinh^2 x \sin^2 y} + j \frac{\sin y \cos y}{\quad}$$

$\cosh^2 x (\cos^2 y + \sin^2 y) - \sin^2 y$

$\cosh^2 x - \sin^2 y$

or

$\sinh^2 x(\sin^2 y + \cos^2 y) + \cos^2 y$

equal

$= \sinh^2 x + \cos^2 y$

this agrees with top of p. 103

$$= \frac{\frac{1}{2} \sinh 2x}{\frac{1}{2} \cosh 2x + \cos 2y} \textcircled{+} j \frac{\sin 2y}{\cosh 2x + \cos 2y}$$

this sign differs from page 103

And otherwise agrees.
& this is slightly simpler

$\cos^2 y = \frac{1}{2}(\cos 2y + 1)$
$-\sin^2 y = \frac{1}{2}(\cos 2y - 1)$

$\sinh^2 x = \frac{1}{2}(\cosh 2x - 1)$
$\cosh^2 x = \frac{1}{2}(\cosh 2x + 1)$

note, just noticed that this result is given as 655.3 on p. 145 of Dwight, Tables

2/16/66 6:25 PM

answer from p. 103 is this

$$F_0 = \left(\frac{b}{\alpha^2+\beta^2}\right)\left(\frac{\alpha\sinh\alpha L + \beta\sin\beta L + j(\beta\sinh\alpha L + \alpha\sin\beta L)}{\cosh\alpha L + \cos\beta L}\right)$$

also, $\alpha^2+\beta^2 = r = \sqrt{1+\omega^2\tau^2}$

Can now get modulus of F_0

$$|F_0| = \left(\frac{b}{r}\right)\frac{\sqrt{\qquad\qquad}}{\cosh\alpha L + \cos\beta L}$$

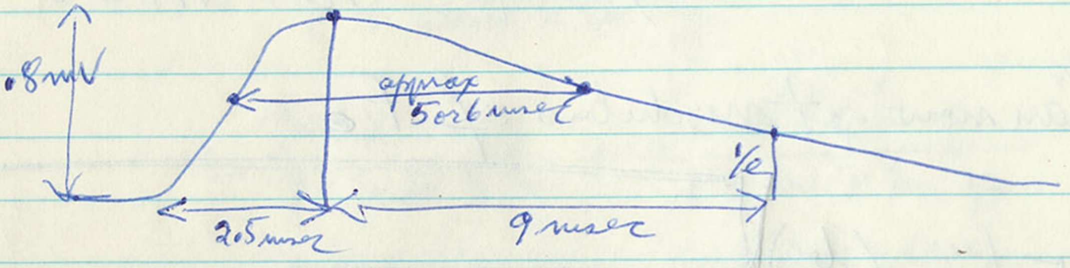
numerator squared $= \alpha^2\sinh^2\alpha L + \beta^2\sin^2\beta L + \cancel{2\alpha\beta\sinh\alpha L\sin\beta L}$
$+ \beta^2\sinh^2\alpha L + \alpha^2\sin^2\beta L + \cancel{2\alpha\beta\sinh\alpha L\sin\beta L}$

$$= (\alpha^2+\beta^2)(\sinh^2\alpha L + \sin^2\beta L) + \cancel{4\alpha\beta\sinh\alpha L\sin\beta L}$$

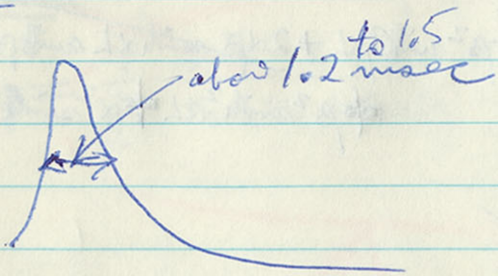
$$\therefore \text{modulus of } F_0 = \frac{b\sqrt{(\alpha^2+\beta^2)(\sinh^2\alpha L+\sin^2\beta L)+\cancel{4\alpha\beta\sinh\alpha L\sin\beta L}}}{r(\cosh\alpha L+\cos\beta L)}$$

Also Bob Burke now has ~~an~~ some excellent unitary slow (dendritic) epsp's?

Slowest is like this



fastest



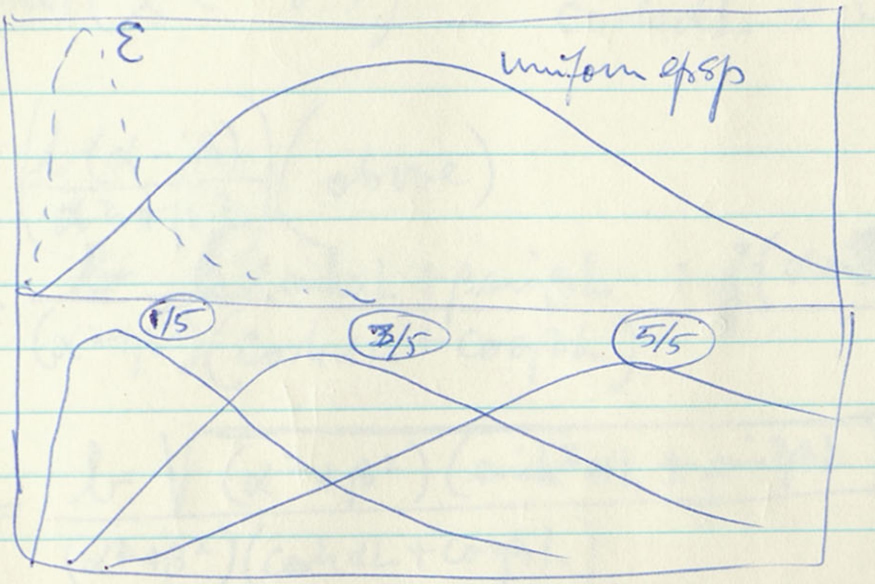
In my 645.1 - fast trans, 10 cpt. series -

time from rising halfway to falling halfway $\tau = 4$ $\tau = 5$

.294 $\tau \simeq$ 1.2 msec for fast in ① 1.47

1.458 $\tau \simeq$ 5.8 msec ⑩ 7.3

2/17/66 Talked with Phil & Bob.
Phil will help me plot figures tomorrow 10AM
They liked the idea of four figures of the type



~~one for~~ Fig. 1 for slow trans & 5 cpts.
Fig. 2 for fast " 10 cpts.
Fig. 3 for square 10
Fig 4 for rounded length variation

Bob Burke's FPL + MG problem see p. 47
& 662. series
I mentioned that got almost no non-linearity with
my cpts ② & ⑤
Bob's suggestion was to have fast one be uniform.
in order to get more non-linearity
farther out.

Try fast transient with uniform
& cpt. 5

2/17/66 from pp 103 & 105

$$\tanh\left(\frac{L}{2}(\alpha+j\beta)\right) = \frac{\sinh\alpha L + j\sin\beta L}{\cosh\alpha L + \cos\beta L}$$

$$F_0 = \left(\frac{b(\alpha-j\beta)}{\alpha^2+\beta^2}\right)(\text{above})$$

$$= \frac{b\left[\alpha\sinh\alpha L + \beta\sin\beta L + j(\alpha\sin\beta L - \beta\sinh\alpha L)\right]}{(\alpha^2+\beta^2)(\cosh\alpha L + \cos\beta L)}$$

$$\text{Mod}\,F_0 = \frac{b\sqrt{(\alpha^2+\beta^2)(\sinh^2\alpha L + \sin^2\beta L)}}{(\alpha^2+\beta^2)(\cosh\alpha L + \cos\beta L)}$$

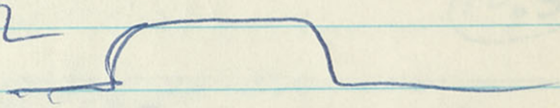
$$= \frac{b\sqrt{r\left(\frac{1}{2}(\cosh 2\alpha L - 1) - \frac{1}{2}(\cos 2\beta L - 1)\right)}}{r(\cosh\alpha L + \cos\beta L}$$

$$= \frac{b}{\sqrt{2r}}\frac{\sqrt{\cosh 2\alpha L - \cos 2\beta L}}{(\cosh\alpha L + \cos\beta L)}$$

2/18/66 Worked out plotting scales for plotting with Phil, who did not come in morning. Also, worked out differences synoptic current − loss current for 661.121 & 661.164 which are to be plotted into a single figure.

Did plot afternoon 2/18/66

Now go over 664.400 Mod. 1/20/66

which worked for 

look back to p. 82

Need to set up 664.414 fits ① E has to go down to .1 at T = .23

664.424 ① E has to go down .30

664.434 E has to go down .46

664.444 E has to go down .83

100. .01 1

1. T .1

These punched up late 2/18/66

2/21/66

Got back 664.404 series setup p. 112

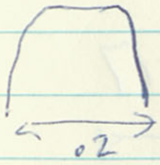
664.414 found $\lambda_{013} = 19.13$ got epsp peak = .1000

initial $\lambda_{013} = 20.$ got epsp peak = .1034

previous 25. .1218

T = .23

664.424 found $\lambda_{013} = 6.954$ .1000



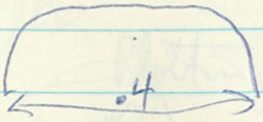
initial $\lambda_{0,13} = 8.0$ .1123

previous $\lambda_{013} = 10.$ .134

T = .30

664.434 found $\lambda_{013} = 3.183$ .1000

T = .46



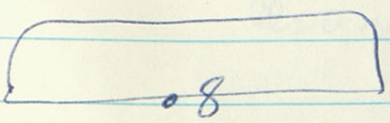
initial $\lambda_{01,3} = 3.0$ .09491

previous λ_{013} = ~~3.183~~ ~~.100~~

4.0 .1218

664.444 found $\lambda_{013} = 1.815$ .1000

T = .83



initial $\lambda_{013} = 1.80$ .09926

previous 2.0 .109

Did a tracing plot of these results.

Still need to do some quantitative measurements

2/24/66 Setup cleanup computations.

✓ 645.100 do to T = 2. set Koppa 6
(later redo as 655.1 for slow trans.)

✓ 645.140

✓ 645.111

2/25/66

✓ 661.165 } can drop 1 & 18 but not 6, 16, 17 & new 19
✓ 661.127 } + 444

also one of 664.414 more time, ~~got for also plot also~~
& 556.1 out to 2.0

Gimmick suggested by Marj. to make 19 gone 16-17
have to use Koppa & Sigma f dependence
because ~~need~~ & inverse f dependence

⑲ = ~~9.86 ⑭ 1 − 9.86~~
= 9.86 ⑭ [illegible] − 9.86 ⑭ ⑥
+ 25 (⑤ + ⑦) − 51 ⑥

Marj says, make Koppa 19 dependent upon 6

then $\sigma_{19,14} = \frac{9.86}{⑥}$ indicated as neg f dependence

$\sigma_{19,\,5 \text{ and } 7} = 25 / ⑥$

$\sigma_{19,12} = -9.86$ ⑭

but see p. 117
not necessary to do this

2/22/66 Washn Birthday

Talked with Jose about his O_2 release, diffusion etc.

Worked on computed epsp write up.

Today, expect Bob Burke to help with a figure (plotting)

For April 11 – Neurophysiology Club at Atlantic City –

Belmont Farley asks for 30 min on dendrites

Present plan ≈ 1/3 to 1/2 on epsp computations

1/3 to 1/2 on dendrodendritic story

1/3 comments on passive vs active dendrites.

Especially give figure relating synaptic & other currents to epsp.

? Maybe on detectability at soma of conductance change in dendrites.

Also, must write J. B. Best & Toni Keiser

2/23/66

For figures

Plotting with Bob Burke is to be 645.1 ①, ④ & ⑧ or ⑩

Should get much longer time (without plot) for 1/10 645.1 series
also uniform case
& 4/10 case
for trans.

Need to set up

Also need uniform slow trans
& 1/5 of slow trans

Also 661.121 } need ~~for~~ more time for currents
661.164 } can delete ① & ⑱

maybe add ⑯ – ⑰ as ⑲

16 $\left[\begin{array}{l} \sigma_{19,12} \quad 9.86 \times ⑭ \quad \text{instead of } \sigma_{16,12} \\ \sigma_{19,14} \quad -9.86 \times ⑥ \quad \text{instead of } \sigma_{16,6} \end{array}\right.$

$\left.\begin{array}{l} \sigma_{19,7} \\ \sigma_{19,5} \end{array}\right\} \quad 25.$

$\sigma_{19,6} \quad -51.$

2/25/66

Finished setting up computations (p. 115)
Yesterday wrote + revised part of manuscript.
Handling flood of reprint requests for dendrodendritic paper.

* Should get art dept. to heavy up Fig. 5 of dendrodendritic paper, for use in paper with Gordon

Got back late 2/25/66
645.100 longer time
645.140 " "
645.111 " "

2/28/66 Put in early 655.100 for longer time

Got back

Meant for completion of figures

664.414 } reruns
664.444
661.122 } finished figure from these
661.165
556.112

Put back 664.414 + 444 with λ013 fixed
also K_{15} + T_iC. in 444

see 121 for results.

To use Mary's Eigenvalue program

Card 1	5		6				
Card 2	N		99		2	0	1
Card 3	M	N	i	j	λ_{ij},	$\lambda_{i,j+1}$,	----

⋮

col 3 col 4
26

---

eg.	Col 4	Col 9	Col 14	Col 19	Col 25	Col 38	Col 50
	5	5	1	1	-26.	25.	
	5	5	2	1	25.	-51.	25.
	5	5	3	2	"	"	"
	5	5	4	3	"	"	"
	5	5	5	4	"	-26.	
	26						

Also did 10x10 with end terms 25. -51. 25.

& 5x5 6.25 -13.5 6.25

Could also try 645.111 with μ_{ij} 100. $Z_m = 1$
6.25 $Z_m = 4$

2/28/66 & 3/1/66

Wrote fig. 3 legend.

*Tried semilog plots & pealing of slow 1/5 (556.112)
and fast 1/10 (645.111)
and slow 5/5 (556.511)

Got reasonably good peels for these, but ratio of peeled slope to passive slope was greater than I expected.

slope
slow 1/5 gave Ratio over $\Delta T = 1$ of 35 = 12.9×e
5/5 26.5 ≃ 10×e
fast 1/10 45 ≃ 16.5×e

Now from my decay time constant boundary value problem, I expected smaller ratios. But wait ratio 2.718 = e
corresp to ln Ratio = 1
for $\tau = \tau_m$

ln 35 = 3.55
ln 26.5 = 3.28
ln 45 = 3.81

see p.118 of ~~Fadiga & B~~ book 7
Fadiga & Brookhart data gives $\frac{\tau_0}{\tau_1}$ between 5 & 8

& from p. 43 of book 7 that lies between L=1 & L=2

Here, we lie very close to L=2, as we should.

However, before I ~~[illegible]~~ did ln, above, I had erroneously concluded that factors were coming out >10 & was puzzled. ∴ decided to solve for Eigenvalues, to check against my BVP.

Eigenvalue results. $z_m = 2$

5×5 matrix ($\Delta z = 0.4$) with $\mu_{ij} = 6.25$

maybe result of lumping?

got $-1.0, -23.6, -9.6, \boxed{-17.4}, -3.39$

see p. 43 book 7 for $L = 2$ } $-1.0, -3.47, -10.9, -23.2, -40.5, -62.6$

The other 5×5 had an error in card punching (decimal point missing)

The clue was that no eigenvalue ~~as~~ small as 1.0

✗ Reason 1.0 comes everytime is because every λ_{jj} is exactly 1.0 greater in absolute value than the offdiagonal elements of same row or column.

The 10×10 with $\mu_{ij} = 25.$ gave

$\boxed{-1.0}, -98.5, \boxed{-3.45}, \boxed{-66.5}, \boxed{-35.5}, -91.5, \boxed{-10.55}, -80.4$

$-51., \boxed{-21.6}$

The larger ones go off ~~because~~ presumably because of lumping.

However, the smaller ones agree well with B.V.P.

3/2/66 plot ~~measur~~ability of conductance change calc.

Setup E & J ~~together~~ & isolated.

---

also slow & fast EPSP — look back to p. 60 + p. 47 662. series

Plan to make slow EPSP fully distributed.

✓

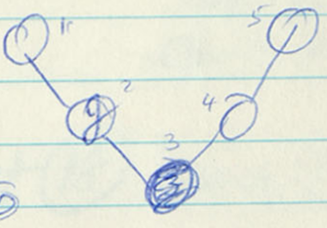
662.101 Two chain of ⑤ sums
mod. based on Three chain 662.004
made fast transient in ② of five
& slow transient 7, 8, 9, 10 of second five
~~&~~ had summer to take sum.
Next time, will have to sum the perturbations, provided they are the ones we want.

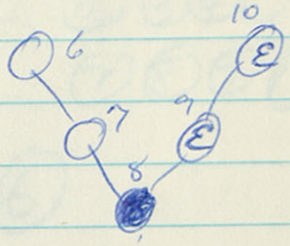
✓

662.200 series following from 655.900 series.

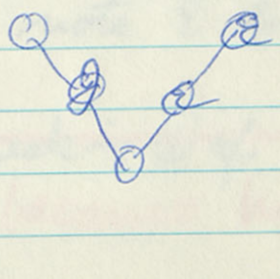
✓
662.201

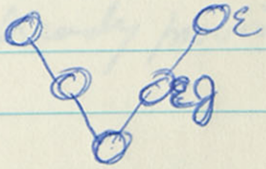
$\lambda_{13,14} = 5.$
slow J = 10 in ②
fast E = 1.00 in ⑨ & ⑩





662.202





Replot (trace 664 series for figure)

Setup 646.135 .136 etc for plot

Rasmussen recommended 1933 article by Lorente de No

Studies in Hearing
in Laryngoscope

as excellent.
He has pursued ideas from this for many years.

He said that Lorente's switch from anatomy to physoology was economically motivated. He said that throughout the 30s & 40s, there was no interest & support of such anatomical studies. In the early 30s it was hard to get any kind of job. All except a few neuroanatomists took up oscilloscopes. A bare 13 neuroanatomists established the Cajal club, which met before the main Anatomy meetings & only very recently began to have a big attendence.

3/3/66 Wrote in memory – also letters.
Talked with Rasmussen in afternoon (Maunen / also Lorente)

Got back 662.101 separate { fast ε = .85 in ②
slow ε = .1 in ⑦⑧⑨⓪ }
see previous page of p.47 & 60

here peak ① was $v = .022$ or 1.55 mV at $T = .24$

peak ⑥ was $v = .0111$ or .778 mV at $T = .60$
too small

increase slow ε peak to .16

add monitor of cpts 12 & 14

setup 662.102 with ε = .85 in ②
slow ε = .16 in ②③④⑤
& " " " ⑦⑧⑨⓪

✓

also let ⑱ have ① – ⑥

Got this back dated 3/4/66 studied 3/7/66 note ε alone in ② already provided by .101

~~Here combined ε gives peak in ① of~~
Did not run because had two $\lambda_{17,2}$ one for each ε
better change one to $\lambda_{19.2}$

3/4/66

Got back 646.135 successful for 1, 6, 11, 17, 18

put in 646.136 ✓ for 3, 8, 13, revised 17, 18

also setup 646.137 ✓ step only 1 & 3

Also got back 662.201 see p. 122

slow J peak = 10 in ② gives epsp peak in ③ of −.04014 −2.08 mV
at T = .64

fast E peak = 1 in ⑨ & ⑩ gives epsp peak in ⑧ of +.0344
at T = .24
2.41 mV

Summer ⑲ starts pos. then goes neg.

plotting scales were off.

desirable to delay E in later problems

also, probably should monitor ② & ④, ⑦ & ⑨
& currents

Put in 662.202 this is 201 with scale fixed & monitor $\overset{14}{J}$ & $\overset{20}{J}$ current in ②

.203 this is 1st chain E in 1 & 2, J in 2
2nd chain E in 9 & 10, J in 7
here 19 sums on J current in ⑦
20 " ②

Phil telephoned 3/7/66

will try to see end of week

should talk with him when get to anom. rectification.

setup 662.204 with E delayed to T=.2

& second chain has sum.

Setup redo on 662.203
662.102

3/7/66

got back 662.102, needs one of two $\lambda_{17,2}$ changed to $\lambda_{19,2}$

646.136 This is part of series for ISTP & TRNSE figure.
Gives cpts 3, 8, 13, & $\{\boxed{17} = \frac{1}{2}(3-8)\}$; $18 = 13 - \frac{1}{2}(3-8)$
had 244 data points
Kappa 18 = 10.

646.137 single chain early part of stop in ① & ③ plus control.

The above two were successful.
Can now prepare figure.

662.203 TRNS E + J Two chains.
Got dependence diagnostic
No R(20, 2) in parameter list
Apparently $\tau_{20,2}$ was inadvertently omitted.

662.202 here $\tau_{20,2}$ was O.K & plots now O.K.
But there was no time change & something funny happened at T = 2.0
Summer 19 gives arith. sum of epsp & ipsp
Summer 20 gives synaptic current at ② for J alone.

time exceeded, put in time factor

worked O.K. for E & J separate, ~~both~~
also arith sum for both starting at zero.

Next, delay E to T=.2

3/7/66

Completed figure for conductance distortion of step in ① & ③ of 5 based on 646.135, 136, 137

Tom Reese stopped in. He has done serial reconstruction of all endings in a small volume of EPL near MBL.

Of 50 endings so studied.

≈40 end on mitral secondary dendrites.

of these ≈30 contained 1 M→G and 1 G→M
~~3~~5 " 2 " 1 "
≈8 " only M→G and seemed to be toward tapering ends of secondaries

3 were endings from unknown source ending upon granule dendrites.

2 were endings upon endings, rare, need further study

? wonder if these are mitral axon collaterals?
Even if so, the others are much more numerous.

662.204 time delay of E in ⑲ & ⑳
⑲ adds ③ & ④
⑳ monitors current in ②
↓ neg peak = −.70 at T = .14
when ③ equals −.01336

puzzled why this neg-current peak + .695 at T = .12
is greater in abs. value than
for ⑲ of 203 where driving pot.
should be a little greater.

✓ put in .205
which is like .203 but with time delay of .204

662.103 Two Chain EPSP Sums
the fast E peak .85 in ② control is provided
1.55 mV at T = .24 by earlier run .101
here ① gives this plus slow E in 2, 3, 4, 5
whereas ⑥ gives slow E only in 7, 8, 9, 10
& ⑱ gives ① − ⑥

peak in ① is 2.43 mV at T = .36
⑥ 1.24 mV at T = .60
⑱ 1.53 mV at T = .24

implying only .02 mV discrepancy

at T = .36
⑥ = 1.034 mV
→ = 1.428 mV
arith Σ = 2.462
only 1% larger

3/8/66 Gotback

✓ 662.103 needs to be rerun with $\lambda_{0,16} = -1.28$

✓ 662.203 needs to have one dependence relation deleted

✓ 662.204 error in data card needed correction

Jose's talk this morning on Liapunov's direct method. Previous time he dealt with theory. Today he presented some examples.

Now work on paper. fig legends, text

3/9/66 worked on Fig. legend & text for "impedance" distortion.

Gotback computations in afternoon

662.203 E+J two chains.

monitored by 20

③ has slow J in ②, faster E in ① & ② same side

⑧ has slow J in ⑦ " " ⑨ & ⑩ opposite side

monitored by 19

pos peak = .47 mV at T=.12 | pos peak = .75 mV at T=.16

neg. extreme = −1.81 mV at T=.76 | neg. extreme = −1.25 mV at T=.92

⑳ neg extreme = −1.008 at T= .12

⑲ neg extreme = −.624 (dv/dT) at T= .12

when ⑧ equals + .0095

bigger driving pot for J in ② here, than in ⑦ here

Compare 0.1% on p.60 But Bob Burke got >10%

with regard to cancellation of E_ε from Ojai paper

$$\dot{v}_i = \sum \mu_{ij} v_j + f_i$$

or, dropping subscript i & treating J = 0 we get, for each i

unit E_ε

$$\tau \dot{v} = \frac{dv}{dT} = \boxed{\tau \sum \mu_{ij} v_j} + \varepsilon 1_\varepsilon + \chi$$

or, if $\mu_{ij} = 5$, would have & $n = 5$

$$\begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{pmatrix} = \begin{pmatrix} \boxed{-6} & 5 & & & \\ 5 & -11 & 5 & & \\ & 5 & \boxed{-11+\varepsilon} & 5 & \\ & & 5 & -11 & 5 \\ & & & 5 & -6 \end{pmatrix} + \begin{pmatrix} \chi \\ 0 \\ \varepsilon 1_\varepsilon \\ 0 \\ 0 \end{pmatrix}$$

for the case of current applied to ① and (ε in ③)

where it is important to remember ε is a fcn of time.

We have here a linear system with a time ~~variable~~ varying coeff + a varying forcing function.

See p. 136

3/10/66 – 3/11/66
Working on a manuscript. Also started bibliographic set of cards.
re
→ accuracy of
cancellation effect for $E_\epsilon = E_r$

Compare compartments ⑰ & ⑱ of

656.514 where $E_\epsilon \overset{0}{=} E_r$ } slow E
with 656.513 $E_\epsilon = 1$ } in ⑤

compartment ⑰ which is $\frac{1}{2}$(① − ⑥)
agrees to all 6 sig. figures for all T

compartment ⑱ agrees for all except the very small values → ⑪ − $\frac{1}{2}$(① − ⑥)

656.514	⑱	686.513
$.279397 \times 10^{-6}$	T = 1.05	$.283122 \times 10^{-6}$
$.109151 \times 10^{-4}$		$.109151 \times 10^{-4}$
$.689889 \times 10^{-4}$		$.689887 \times 10^{-4}$
$.219814 \times 10^{-3}$		$.219814 \times 10^{-3}$

all agree from here on

∴ error as fraction of ⑪ which ≈ .3
is factor ≈ 10^{-8}

This small error due either to computer or to Moses program, because the computations themselves are independent.

In other words. Applied current must not, itself, change any coeff. Thus, anomalous rect. would not be permitted.

If present, how fast does it develope?

The result of rights comes from linearity of the system & does not require coeff. to be time invariant, provided they are identical in both trials.

Hence extension to compartmental system can be inferred, for system shown on p. 133.

3/11/66

for an isolated compartment, we would have

$$\frac{dv}{dT} = -(1+\varepsilon)v + \varepsilon 1_\epsilon + \chi$$

If we set $E_\epsilon = E_2$, which here means $1_\epsilon = 0$, then get

$$\frac{dv}{dT} = -(1+\varepsilon)v + \chi$$

If, instead, we subtract two cases, with same $\varepsilon(t)$ we get

$$\frac{dv_1}{dT} - \frac{dv_2}{dT} = -(1+\varepsilon)(v_1 - v_2) + (\varepsilon 1_\epsilon + \chi_1) - (\varepsilon 1_\epsilon + \chi_2)$$

or, setting $y = v_1 - v_2$, we have

$$\frac{dy}{dT} = -(1+\varepsilon)y + (\chi_1 - \chi_2)$$

~~If we set~~ If $\chi_2 = -\chi_1 = -\chi$, then $v_1 = -v_2$ & $y = 2v_1$ & we can divide thru by 2 & get

But actually, cancellation of E_ϵ, and for that matter also E_j does not depend upon $\chi_2 = -\chi$.

In general $\frac{dy}{dT} = -(1+\varepsilon+\beta g)y + (\chi_1 - \chi_2)$

where y corresp to v with $E_\epsilon = E_j = E_2$, and $\chi = \chi_1 - \chi_2$

The point is that the E_ϵ & E_j contributions are in the forcing term, and ~~the~~ superposition holds for the forcing term if not for the perturbation of the system itself.

This trick does depend upon $\varepsilon(E_\epsilon - E_2)$ being the same in both cases. also, matrix being same in both cases. see left.

For approximation, could ~~suppose~~ consider $C_1 \doteq C_p = X$

Then $C_p \cong B_p + D_p$ goes

$$X = B_p + X V_p$$

$$X = \frac{B_p}{1-V_p}$$

For 646.130 – 137, where we have all the numbers, contr this.

$U = .4051$
$L = .2635$

$U+L = .6686$ $U-L = .1416$
$V_p = .3343$ $B_p = .0708$

$$X = \frac{.0708}{.6657} = .1063$$

whereas $C_1 = 0.098$ ~~and~~ at $T = 1.04$, have C_{1+} 0.101
$C_p = 0.105$

Now $(.101)(.3343) = .0338 \simeq D_p$
$.0708 = B_p$
$.1046 \simeq C_p$

close ✓

whereas $(.098)(.3343) = .0327$
$.0708$
$.1035$

a little low, but not bad.

∴ put in 646.555 to obtain necessary control.

3/14/66 – 3/15/66

Writing "distortion" due to dendritic conductance change part of paper. Note, most of computations do not have the control step transient in the perturbed compartment, & hence, I do not actually have the ΔV peak, with $E_\epsilon = E_r$, in the perturbed compartment.

Assuming my general interpretation is correct, these distortions can be estimated as follows & if desired, could be checked out.

Let U = upper dashed curve in pert. cpt.
L = lower " " " "

$V_p = \frac{1}{2}(U+L)$ = control v peak " " " in absence of current step.

$B_p = \frac{1}{2}(U-L)$ = distance from baseline to peak of dotted curve for $E_\epsilon = E_r$, and presence of current step.

But this does not give amplitude of control step at time of v peak, nor distortion from it to dotted peak. $\equiv D_p$

time of peak $\cong$ 1.04

Let C_1 = control step amplitude at $T = 1.0$
& C_p = " " " time of peak.

By definition $\boxed{B_p + D_p = C_p}$

Then, we estimate that $D_p \simeq (C_1)V_p = (C_1)\left(\frac{1}{2}(U+L)\right)$

$$B_p = \frac{1}{2}(U-L)$$

$$C_p = B_p + D_p \simeq \frac{1}{2}(1+C_1)U - \frac{1}{2}(1-C_1)L$$

see left.

3/16/66

Result of 646.555 for current step at ① observed in all five compartments. Examine v at several times.

	T=1.0	1.04	1.09
①	.2664	.2697	.2736
②	.1627	.1659	.1696
③	.09808	.10097	.1044
④	.06091	.06351	.06666
⑤	.04404	.04647	.04943

3/23/66

Spend afternoon with Bob Burke.
We plotted two evoked epsp & one miniature.
Got little encouragement

The afterpotential louses things up.

for amplitudes below 20% of peak amplitude, it seems that semilog slope gets steeper than from 100% to 20%.

This might seem to be faster decay, but it is more likely afterpotential, maybe due to some K or Cl permeability increase.

Only real way to handle this is to provide a theory which also accounts for the afterpotential.

Bob did say that he does have some more obvious two stage decays, but he thinks that inhibition is involved in these.

↑
disynaptic

3/16/66–3/17/66 pressed on with manuscript & xerox of same
prepared sketch figures to permit taking original
pencil drawings to art dept.
wrote Dissection of currents.

3/21/66–3/22/66 Ainsley Iggo's visit & took him to
Baltimore. Saw Mountcastle, Davies,
Brindley & a mathematician engineer
from APL ? Viernstein

3/23/66

On Monday (3/21/66) while showing Ainsley around, I told Bob Burke about my equalizing time constants & that some of his best data would be very suitable, and that this provides evidence for Ƶm. He was very surprised that this would be independent of location. I told him he should peel some of his epsp on semilog plot. Plan to talk to him & Phil about it today & maybe write short memo.

The more I think about, the more I think this deserves priority. My manuscript on these time constants must be polished off. present title is

But consider ~~Decay time constants~~, e
~~Decay and~~ Equalizing Decay Time Constants and Dendritic ~~Electrotonic~~
Length of Dendritic Trees.
Possibly even suitable for mention at conference.

Theoretical

levels

Experimental

vague concepts & hypoth — qualitative — early expts.

more explicit physical intuitions & some crude theory — semi-quantitative — better expts, more comprehensive data.

quantitative

explicit math model ⟷ improved instrumentat more comprehensive & precise observations

↓ detailed predictions some of which are very hard to test

Can have much greater generality here & become specific with specific values of the parameters.

improvements can be of at least two kinds

(1) greater control & precision with few variables

math models are especially needed here. → (2) greater comprehensiveness in including many variables

↑ great need here.

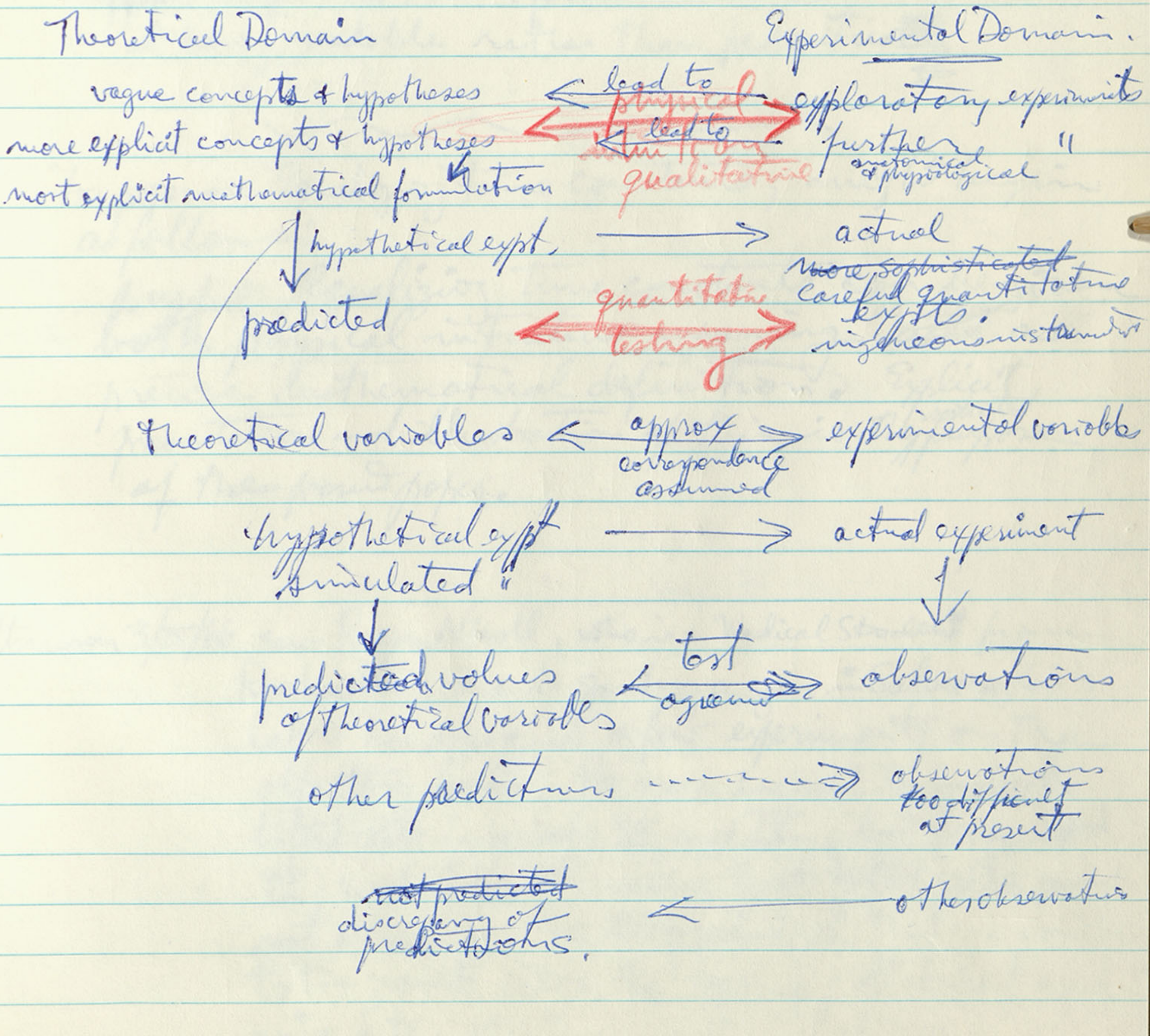
I can enjoy spending almost full time in this abstract universe. But exptl. contact helps to keep at least one foot on the ground.

When certain detailed predictions are not fulfilled experimentally, we must ask: is this a trivial discrepancy or a valuable clue? If it is not trivial, is the theory all wrong, or can one pinpoint a wrong assumption, or a failure of expt. to satisfy conditions that were assumed. In other words, what kind of mismatch is responsible? The crux is to pinpoint the mismatch and to judge its significance.

3/24/66 - 3/25/66

Think about NINDB Council presentation next Wed., March 30. Phil, Bob & Tom will present some of their material from this overall joint effort, & K invited me to contribute also.

Believe it would be a good idea to give part of time to making the distinction between Theoretical Domain & Experimental Domain



Theoretical Domain — Experimental Domain.

vague concepts & hypotheses ← lead to → exploratory experiments

more explicit concepts & hypotheses ← lead to → further anatomical & physiological "

~~physical~~ qualitative

most explicit mathematical formulation

↓ hypothetical expt. → actual ~~more sophisticated~~ careful quantitative expts. using neurons instruments

predicted ← quantitative testing →

theoretical variables ← approx correspondence assumed → experimental variables

hypothetical expt "simulated" → actual experiment

↓ ↓

predicted values of theoretical variables ← test agreement → observations

other predictions ⇢ observations too difficult at present

~~not predicted~~ discrepancy of predictions. ← other observations

3/25/66

Must plan slides for Wed & for April 11

In the EPSP paper, may want a very early paragraph, headed

Theoretical domain and experimental domain are fundamentally distinct. This distinction deserves explicit attention, because it can sometimes appear to get lost in a presentations which aim at being readable rather than pedantically

For paper on Equalizing time constants, might begin as follows:

Equalizing time constants can be given ~~both~~ a useful physical intuitive meaning ~~and~~ as well as a precise mathematical definition. Explicit presentation and illustration of this is the restricted purpose of ~~the~~ present paper.

Afternoon 3/25/66 saw Roger Nicoll, who is a Medical Student from Rochester, who is spending a year in Salmoraghi's lab & has done quite a few experiments on the olfactory bulb. He was inclined to implicate tufted cells in periods III and IV, but for period III, he had come to realize that tufted cells could not account for the deep potential that we ascribe to the granule cells. He seemed pretty bright and up to date with the recent literature.

148

3/30/66

Together with Phil, (& Barbara Alving on Aplysia) Tom, Bob Burke & K. F. — we presented some of spinal cord work to the Scientific Council of NINDB — Walsh, Denny-Brown, MacNichol, Woolsey & ? ~~pharmacol. biochemist.~~ → Abood who knew Zim.

I was last & others had all presented argument as starting from soma & gradually establishing experimentally that the soma picture was not enough — sort of getting out into dendrites by induction.

① I pointed out that MR purely theoretical & that contact with spinal cord section helped me keep one foot on the ground.

② I pointed out that research depends upon our expecting something from ~~our~~ experiments: an expected result is satisfying, but an unexpected result can be very valuable. Physical intuition But then, as expt. get more complicated, more quantitative and sophisticated, our physical intuition is no longer a sufficiently reliable or quantitative source of expectations — this is where mathematical theory becomes essential. Then one can explore in detail, what would happen if such & such & if we do so & so ~~under~~ these particular condition. Computer can answer to six significant figures.

③ Whereas the others presented their results from the point of view of the soma & working out to discover the dendrites; my approach has been (since 56) to assume the importance of the dendrites, and explore the implications in quantitative detail.

Then quickly went thru slides
① tree to equiv. cylinder transformation — spread from soma to dendrites; dendrites to soma
② diagram of two compartments
③ Fig. 6 of Ojai paper
④ fast trans EPSP in ten cpts. of present paper
⑤ step trans & EPSP to obtain distortion.

for future make a single slide

3/30/66

There were a number of questions from the Council, when Tom spoke — showing doubts about the impedance approach. I think, especially in view of Tom's objection to my word "distortion", that the paper should make a more clearcut distinction between Tom's experiment and my experiment.

Also, the equalizing business was pointed out in talk and should be pointed out in paper.

Must now concentrate first on necessary slides for April, then on finishing writing paper.

Tree → equiv. cylinder fig — $Z_m = 1$ for $R_m/R_i = 90$ cm ≈ 80 ≈ 1000

$\therefore Z_m = 2$ for $R_m/R_i = 22.5$ cm ≈ 25 ≈ 20

But of course, dendrites themselves can be longer.

R_m/R_i 80 could be $\frac{4000}{50}$ or $\frac{8000}{100}$

R_m/R_i 20 could be $\frac{1000}{50}$ or $\frac{2000}{100}$

Equiv. cylinder is ~~8" long~~ 7 3/4" chain of 5 goes x on 1 1/2" centers 3/4" in from each end,

chain of 10, 3/4" centers, 3/8" in from each end.

Also, for Figs 1 & 2 of Bulb presentation, must check back.

Slide Sequence used (20-25 minutes) fairly fast

1. Schematic summary of assumptions; tree to cylinder to chain of cpts.
2. TRNS E, Uniform EPSP; Three non-uniform EPSP
3. Synaptic current, spread current, net depol current
4. O-Bulb – Phillips, Powell & Shep. exp setup & results
5. Schematic Golgi plus 4 records with 3 time periods
6. Schematic mitral abstraction & bulb abstraction
7. Computed mitral antidromic, intracellular & two extracell
8. Granule field computation
9. Schematic Golgi plus serial reconstruction of Gemmule

Use as prop. for concluding remarks.

At this point, developed argument and conclusions reached, to provide basis for orientation during next few slides. This proved to be important.

Zim had noted, during dry run, that confusion could result without this.

4/28/66 Dieter Lux dropped by.
He is about to return to Munich
He & Phil did some AC driving of motoneuron.
✱ They could use my solution that includes the coupling resistance.

4/5/66 Slide preparations were completed 4/1/66 – 4/4/66
Should be ready from photography late today.
Also cleaned up numerous small chores.
Have been fighting virus cold for about week.

4/7/66 Did a useful dry run of talk with Jim, Jose, Manes & Marj. as audience

4/13/66 Got back from Atlantic City symposium. There were about 300 Neurophysiologists in attendance. Symposium was well received. One question after my talk was about non-alignment of $\oplus$ in $\ominus$ in period I. I think Another was on symmetry of tree. Another had to do with passive granule cells. Saw Kathryn Green (Thomas) who seems to be interested in further study of dendrites & testing (14) assumptions. Wohlbarsht said he thought he had some relevant data. Llinas said he was working with frog cerebellum & might wish to discuss some of the interpretations. Talbot (from Seattle) said he has also worked on cerebellum & he disagrees with some of Eccles interpretations. I did emphasize reference electrode & the intracellular & extracellular current flows. I did emphasize independence of ~~studies~~. Woodbury said Patton is now Prof. & asked if I would visit sometime. I talked to Cole on way up & learned about his Senior Research Scientist position & Berkeley Professorship combo; he had enjoyed Falk & Fatt paper.

He also brought up elliptic vesicles of Uchizono and recently? Bodian

At Philadelphia, had good visit with Farley, Gerstein, Harmon, Lewis, Crain. Farley & Gerstein happy there; Lewis's group mostly broken up. Crain at Einstein.

4/12 – 4/16 Shepherded Keith MacLeod around N.I.H.
4/20 – 4/21 Sick leave to finally get over flu.
4/25 – 4/29 Short version of annual report. Correspondence.
Straighten & sort tremendous pile of Journals, reprints & junk mail & Sciences piled up on desk & tables.
Clearing decks for getting back to writing.

At College Park – Met Larry Goldman UCLA Ph.D. conduction velocity + diameter
Harold Gainer
Wolfgong M. Schleidt turkey behavior
? fish behavior

There was some discussion + interest in dendrodendritic synapses & notion that these dendrites could remain passive.

One man (fish behavior modeler who is doing some work with Harmon's neuromime) got the idea that my compartmental method should give a sum of exponentials.

Goldman had not realized that I have the transient solution for the finite cylinder. He also did not realize that I had $K \neq 0$ case to cover different branching laws. He thought I was stuck with equivalent cylinder.

He cited Weidman as having published the steady state solutions for finite cylinder. Will check this He just gives these solns as from Hodgkin & Huxley, who suggested project.
perhaps J. Physiol (1952) 118 348 ✓

He said that Grundfest runs a post-doc technician factory in his loft.

Goldman thinks my finite cylinder results should be brought out. He definitely thinks there is more need for further communication of these results.

5/2/66

Plan slide sequence for 45 min talk at College Park

1. Three Cajal neurones
2. Microelectrode in Soma
3. Transient response to step: limiting cases
4. Cajal neurones & schematic neurones (synapses)
5. Schematic assumptions; tree to cylinder to chain
6. Four dendritic locations
7. Two spatiotemporal sequences

---

8. O-Bulb; Phillips, Powell & Shep. exp. setup & results
9. Schematic Golgi plus 4 records (3 time periods)
10. Schematic mitral abstraction & bulb abstraction
11. Computed mitral antidromic V_i, V_e two ref.
12. Computed granule field " " " "
13. Superposition
14. Schematic Golgi plus 4 records
15. E.M. low power, mitral sec cross, granule long.
16. high power pair of contacts
17. reconstruction from serial sections
18. Schematic Golgi plus serial reconstruction

5/2 – 5/6 66 This week, cleaned up several correspondence chores. Also did referee job. Took care of setting up seminar for Dork Work with Lloyd Guth. & Gave talk at College Park & talked with Group.

Katz & Thesleff compared muscle epp in fibers of different diameter & correlated this with the measured input resistance. They found ~~a~~ a pretty good, but not perfect proportionality.

This depends upon the ΔG_E being small enough that $\Delta R_E = \frac{1}{\Delta G_E} \gg$ input resistance.

Both Martin & Katz & Thesleff treat the epp peak as a purely resistive phenomenon. They neglect capacity & reactance of the input impedance.

\# Thus, there is a need for a better treatment. I could use a modification of the N.Y. Academy treatment.

Or I could do compartmental computation.

In fact, I already have some compartmental computations for a branchlet, which do show an effect of this kind. See p. 160

The Russian contribution is to combine this effect with the Lorente de Nó & Condouris decremental conduction & branch node effect.

5/9/66 (dating back several weeks)
Loose notes re my older thoughts about dendritic swelling & growth & more recent thoughts of applying this to gemmule.
If enlargement of gemmule is involved, get both
(A) presynaptic specificity
(B) reinforcement by success on postsynaptic side.
Need to explore more fully how firing together with prolonged local effect would do this. Cf older notes re dendrite & residual current flow $(196\overset{3}{4}?)$
? Relevance of fact that gemmules have lots of vesicles ?

5/10/66 Five Russian reprints from the Inst. of Biophysics, USSR Academy of Sciences, were sent to me by Prof. Y. Arshavskii. At library translation, Mr. P. Deporte translated the titles & one paper for me orally. One is on dendrites, other 4 are on syncitia. The syncitia paper seems to go beyond the case considered by E.P. George Aust. J. exp. Biol (1961) 39 267-274

The dendritic paper emphasizes the idea that dendritic membrane should be active, and that the same synaptic conductance change should produce a larger amplitude of local EPSP out in a dendrite than at the soma, because of the larger input conductance, and that this could initiate an impulse in the dendritic periphery. They got the idea of the enlarged local EPSP from Katz.

Katz & Thesleff 1957 J. Physiol. 137 267-278
Martin 1955 130 114-122

Laplace transforms he did not work them
But should give expressions for
Complementary error fcn
& its derivatives
Similar to footnote on hyperbolic fcns.

1962 - N.Y. Acad Paper

after eqn (6), sentence on V^* would be less puzzling if it referred back explicitly to eqn 2

Also, my note, prefer differ st. st. notation V_{ss}

eq (8) should be explicitly stated to an analytic rather than a graphical result.

p. 1077 - end of top ¶, add for isolated patch ($I_m = 0$).
also two lines before eq. (11) add "total" to internal current.

p. 1079 He still feels that eq (21) does not have its significance sufficiently flagged.
Also, he would like to consider even greater generalization for $e^{z(z-z_0)}$ as some empirical fcn of Z or X, but he did not seem to fully appreciate the difficulty.

5/12/66 Saw Larry Goldman on Thursday afternoon.

He had studied 1959, 1960 & N.Y. Acad. paper to be able to ask me questions & tell me where more ~~helpful~~ details would be helpful to readers like him. He did not mind starting with PDE.

1959 paper. It was not clear to him until he was finished, that the rationale was to find a general method to work out terminal impedance for all possible successive branching. Would like more early briefing on approach.

Also, p.496, would like more explicit treatment of boundary conditions, more like in NMRI report. Not obvious why $B = 0$ & $B = \infty$ correspond to what I say they do.

It would help if $\frac{\partial V}{\partial X}$ were written on p.496, just after V. This would help for B.C. & also for eq. 8 & 9 on p.499, where Goldman says he wasted a lot of time.

eq.(14) could be explicitly pointed out to apply for both branches & also here one can cite ⑩ for $d^{3/2}$

also, this is first place where need R_m const (R_mR_i)

p.506 He wasted a lot of time on 29 & 30. Would help to provide clue let $y = \sqrt{R_m}$, rearrange & solve quadratic for y. Then square.

1960 paper – Appendix p.524 B.C. first eqn may be too much at once

perhaps write out soma current $I_S = V/R_S + C_S \, \partial V/\partial t$

$$= {}^1/R_S \left(V + \partial V/\partial T \right)$$

combined dendritic current for n equal cylindrical trunks would be

$$I_D = \frac{n}{r_i}\left(-\frac{\partial V}{\partial x}\right).$$

(for each branch $I_D = \frac{1}{\lambda r_i}\left(-\frac{\partial V}{\partial X}\right)$)

$$= \frac{n}{\lambda r_i}\left(-\frac{\partial V}{\partial X}\right).$$

$$= -G_D\left(\partial V/\partial X\right).$$

and $G_D = \rho/R_S$

which holds even for cylinders of different diameter.

$$\therefore \; I_A = I_S + I_D = \left({}^1/R_S\right)\left(V + \partial V/\partial T\right) + \left(\rho/R_S\right)\left(-\partial V/\partial X\right).$$

p.525 line 4 should read "steady state" rather than just steady.

~~Kappa 12, 13, 14 to be 1/32~~ should be 1/32

$\lambda_{12} = 8.$

$\lambda_{23} = 1 \times \lambda_{12} = 8.$

$\lambda_{34} = 1 \times \quad 8.$

$\lambda_{45} = 1 \times \quad 8.$

$\lambda_{16} = .25 \times \quad 2.$

$\lambda_{61} = .75 \times \quad 6.$

$\lambda_{21} = .25 \times \quad 2.$

$\lambda_{32} = .50 \times \quad 4.$

$\lambda_{43} = .50 \times \quad 4.$

$\lambda_{54} = 1. \times \quad 8.$

$\lambda_{2,10} = .5 \times \quad 4.$

$\lambda_{10,2} = 1. \quad 8.$

$\lambda_{10,11} = .5 \times \quad 4.$

$\lambda_{11,10} = 1. \times \quad 8.$

$\lambda_{3,9} = .5 \quad 4.$

$\lambda_{9,3} = .5 \quad 4.$

$\lambda_{2,12} = 2. \times \quad 16.$

$\lambda_{3,13} = 1. \times \quad 8.$ → should be 16

$\lambda_{4,14} = 1. \times \quad 8.$ ″ ″ ″

$\lambda_{12,2} = .125 \quad 1.$

$\lambda_{13,3} = .25 \quad 2.$

$\lambda_{14,4} = .5 \quad 4.$

Size $= C_j$

↓

$C_1 = 1$

$C_2 = 1/4$

$C_3 = 1/8$

$C_4 = 1/16$

$C_5 = 1/16$

$C_6 = 3$

$C_9 = 1/8$

$C_{10} = 1/8$

$C_{11} = 1/4$

$C_{12} = 1/32$

$C_{13} = 1/32$

$C_{14} = 1/32$

Real Constraints are that

~~$\lambda_{61} = \lambda_{21}$~~

$\lambda_{10,2} = \lambda_{3,2} = \frac{1}{2} \lambda_{2,3}$

$\lambda_{6,1} = 3 \lambda_{21}$ and $\lambda_{2,1} = \frac{1}{4} \lambda_{1,2}$

Kappa 6 = 1/3

of .8 used ~~as~~ as E battery λ

It was erroneous to make $\lambda_{0,12} = 32. \times \lambda_{12,8}$

should be 1. and $\lambda_{12,8}$ should be 32.

also, better to compare ε in ② & ⑫ ③ & ⑬ ④ & ⑭

in ① 1/2 = ε 2 16 4 16 8 $\varepsilon = 16$

5/13/–5/16/66

finished individual annual report.

Also did some library research.

Now must get back to EPSP paper & Thon Bulb paper.

Partly because may wish to examine synaptic current in such cases.

Checkup on Branchlet calc. – Deck 732.210

dated 11/4/63

This deck was for problem 732.213

Now check back on folder & output

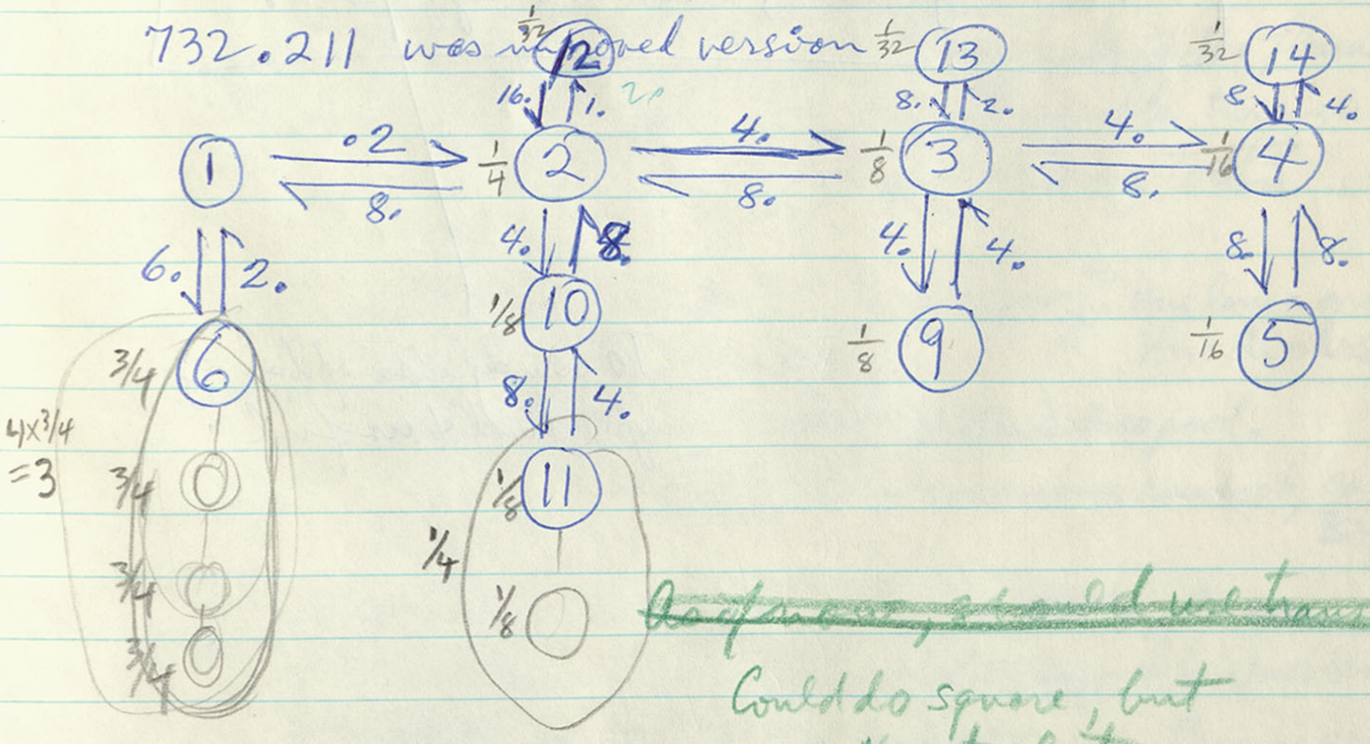
732.201 10/18/63 where had to reduce no. of cpts & add dependence

732.202, 203 errors.

Note, as in Ojai $\mu_{ij} = \frac{g_{ij}}{C_i}$ $\mu_{ji} = \frac{g_{ij}}{C_j}$ for voltages

but in Mones' program $\Big\}$ $\lambda_{ij} = \frac{g_{ij}}{C_j}$ $\lambda_{ji} = \frac{g_{ij}}{C_i}$ for charge

732.211 was improved version



~~[illegible]~~

Could do square, but without plot.

If want voltage, need Kappa$_j \propto \frac{1}{C_j}$

Thoughts about Title. Probably better to start with word, neuron or nerve, rather than theory.

Neuron Theory   Neural Theory

Neuron Biophysics

Neurophysiology in Theory and Practice

Neuron Theory and Practice

Nerve Cylinders and Trees

Nerve Cylinders, Trees and Synapses.

To convey idea of being practical & useful.

Books are instruments of communication, and the only objective test of their success is whether they are bought and read.

5/17/66

An article in Science "Book Publishing — and Bookkeeping"
13 May 1966 — Vol. 152 pp 871–875

Provides some hard headed advice from an editor of McGraw-Hill.

To write a good book takes: (1) competent grasp of subject (necessity)
(2) good planning ← often overlooked
(3) hard work (obvious)

Worst way to write a book is to sit down and start writing. Don't think of writing.

A good book must be built.

need Clear workable concept {
focus of book
what covered
what excluded
purpose served
for whom intended

p. 872 Anticipate book jacket description:

Can you crystallize what the book will do in a single sentence, and so accurately that no customer will be misled?

Will this capsule summary appeal?

Will it promise answers to questions, help to the floundering?

~~ok~~ Are you merely going to conduct a pleasant ramble through your subject, or are you fashioning a working tool?

872 873 Who are the prospective readers? How many? How large a group? How diverse?

Should be able to provide publisher & editor ~~of the size~~ estimate of size of audience pool.

i.e. Neurophysiologists, Neurosurgeons, Neurologists, Gen. Physiol. Biophysics.

872 If the book is to be indispensable to the user, then the needs of user (his level of understanding & his problems) are indispensable to the author. This is a warning against loading the book with too many loose ends of doubtful value. Better leave the book shorter, with possibility of sequel or revised edition later. Not catchall

my note

	①	⑧	factor →
EPSP=.01	$\varepsilon=.256$	$\varepsilon=2.6$	≈10
EPSP=.1	$\varepsilon=2.74$	$\varepsilon=49.9$	18.2
factor ↓	10.7	19.2	

5/19/66

Resumed writing EPSP paper
Decided to setup two computations.

615. modification of 645. Series ~~but~~
only in setting EPSP peak = 0.01

615.010 set $\mathcal{E} = 0.274$ in ① with range

615.080 set $\mathcal{E} = 5.0$ in ⑧ with range

These are just to fit. Then rerun for plot.

5/20/66 Put in 645.161 for long time, to get 50% down point

Got back 615.010 initial $\mathcal{E} = 0.274$ made EPSP come out 7% high

Found $\mathcal{E}$peak = 0.256

Compared with 2.74 for 645.111

Shape of EPSP, with factor of 10 scale change, is negligible: less than thickness of line.

615.080 initial $\mathcal{E} = 5.0$ made EPSP 84% too high
+ v peak in ⑧ nearly twice the value needed.

Found $\mathcal{E}$ peak = 2.6 compared with 49.9 for 645.182

+ v peak in ⑧ = 0.06286 at T = .09

compared with 0.602 at T = .08 in

Negligible shape change in ①

is. 4% change in ⑧

Summary

% increase of v for 10% increase of ε

Perturbed Cpt.	ε for EPSP=.01	v_{pert}		ε for EPSP=0.1	v_{pert}		factor ~
All	.1093	.010	9.94	1.152	.10	9.4	1.053
1	.2558	.010		2.74	.10		1.07
2	.4064	.01123		4.408	.112		1.084
3	.6124	.0154	9.9	6.88 ~~6.965~~	.155	8.8	11.25 ~~1.138~~
4	.8870	.0220	9.8	10.51 ~~10.60?~~	.220	8.1	11.86 ~~1.195~~
6	1.697	.0414	9.6	24.3	.405	6.5	1.433
8	2.602	.0629		49.9	.602		1.92
10	3.08	.1114	9.1%	234.	.940	1.5%	76.0

Results of linearity check for 10% increase indicate that roughly proportional to $(1-v_p)$

more nearly prop to [redacted]

$(1-0.9v_p)$

5/20/66 Put in 615.020 cpt 2
615.100 cpt 10

Got back 5/23/66 Jose del Castillo lectured in afternoon

615.020 initial ε of .4408 gave EPSP=.01084 8% high
Found ε = 0.4064 in ②

615.100 initial ε of 23.4 gave EPSP=.04845 384% high
Found ε = 3.08 in ⑩

Setup 615.030 and 615.040 on 5/24/66

5/25/66
Setup 615.101 testing 10% increase of ε in ⑩ at both EPSP ranges
3.083453 to 3.3918
234.35 to 257.79

615.001 testing 10% increase of ε in all for both ranges.
.1093146 to .12025
1.15202 to 1.2672

Purpose is to characterize linearity + non-linearity at these operating points.

also setup 615.041 with 10% increase

and ~~645.132~~ to correct ε value 615.031 with 10% increase
that gave EPSP 1% too large ← correct later

6/3/66

Seminar: because of many interruptions, only got thru slide 4 on synaptic currents. Several questions came up that may be worth noting.

Right at beginning, Walt Freygang asked whether glia did not make case more like axon in oil than axon in air. My answer is that fact that extracellular amplitudes are less than 1 mv proves that extracellular resistance is much lower than intracellular & membrane resistance. I made this point also in discussion at Farley's home in Philadelphia. It seems to be a point not widely appreciated. Only catch is that Giant Extracellular might be getting inside oily layer, while ordinary extracellular is outside.

Belmont

Walt was not convinced, by visual examination, that Bob Burke's EPSP looked like mine. This emphasizes the need for the quantitative chart.

Also, when I say that shape is constant for all amplitudes, I must be careful to say that I do not mean to imply that summation need be synchronous. Slight asynchrony can change effective shape of conductance transient.

Rapoport wanted to know why G_E & G_I separated. I said G_I represents most of membrane & G_E represents potential active patches.

Also, he wanted to know why conductance rather than current. Answer is non-linearity when it occurs

5/31/66

Got back 615.001 and 615.101 and prepared linearity of E chart.

put in 615.081 & 615.061 good

↑ Trans

6/2/66

setup 615.102 to find peak time of EPSP for fast E in ⑩ but with Zm changed.

So for $Z_m = 2.0$ making $\lambda_{ij} = \frac{100}{\cancel{2}4} = 25$

Compare $Z_m = 1.0$ $\lambda_{ij} = 100$

$Z_m = 4.0$ $\lambda_{ij} = \frac{100}{16} = 6.25$

615.012 for cpt. ①

615.005 for uniform inhibition fct -.05

Now have typed pages 1-1 thru 1-6 of results on subject of slope

2-1 thru 2-2½ " " " E & linearity

Decide if slower E transient causes EPSP moves in to resemble others farther out. This may be worth discussion & pointing out.

Settle about figures & tables & final write up.

See left.

✗ Check over slides for Wade Marshall seminar Friday 5/3/66

use plan similar to Atlantic City & College park see p.151 & p.154

Leave out Cajal & microelectrode trans. slides. Have 15 slides selected. 1-9 exactly same as Atlantic City later called medium

τ/25

from 615.102 - 615.104 &

fixed in compartment ⑩, fast transient -

Zm	Rij	foot	peak time	foot to peak	halfway up	halfway down	halfwidth,
4.0	6.25	.54	1.8	1.26	1.01	3.21	2.20
2.0	25.	.19	0.86	.67	0.42	1.88	1.46
1.0	100.	.09	0.41	.32	0.19	1.21	1.02
				1.6 msec			5.1 msec

615.013 & .014

fixed in compartment ①, fast transient -

E

								E value
4.0	6.25	.02	.135	.115	.045	.405	.36	.1645
2.0	25.	.01	.11	.10	.036	.330	.294	.256
1.0	100.	.01	.10	.09	.03	.30	.27	~~.185~~ .45

Briefly for ⑩ get almost factor of Two

for ① get more like 10% down + 20% up

6/3/66
Got back

615.081 for 10% increase of ε in ⑧ for both ranges
got 9.47% at .01 and 4.62% at .10

615.012 changing λ_{ij} to 6.25 ($i Z_m = 4.0$) made peak occur for ε in ① T = .13
100. = .10
compared with 25. T = .11

615.102 for ε in ⑩ λ_{ij} of 6.25 gave peak time > 1.4 1.8
100. .41
25. reference .86

615.005 uniform fast transient g = 7.85 at T = .18
but now setup for slow transient
found g = 4.045

Setup 655.005 same with slow trans, fit at T = .35

615.103 ε in ⑩ for longer times λ_{ij} = 6.25, 100.
found 1.8 as time of peak

615.082 ⑧ gremlin goofed data cards need to rerun

615.013 fit with Δt = .005 λ_{ij} = 6.25

6/7/66 Got back above four decks .082 had been goofed by gremlin
.103 found T = 1.8 as peak with λ_{ij} = 6.25
.013 for λ_{ij} = 6.25 found ε = 0.1645 in ① for EPSP = .01 at T = .135
full plot
halfway up at T = .045
halfway down T = .405
Halfwidth = .36

Therefore setup 665.002

with $\lambda_{17,2} = 4. \times \lambda_{0,17}$

$\lambda_{2,8} = 1. \times \lambda_{0,17}$

$\lambda_{0,8} = -1. \times \lambda_{0,17}$

dummy set=1 for first time range and zero for second

$\lambda_{18,12} = 32. \times \lambda_{0,18}$

$\lambda_{12,8} = 1. \times \lambda_{0,18}$

$\lambda_{0,8} = -1. \times \lambda_{0,18}$

dummy set equal to zero for first time range and 1. for second.

& for T.C. set $\lambda_{0,17} = 0.$

This correction was recognized as necessary after examing output of 665.001 which yielded

$V_2 = K_2 Q_2 > 1.0$

and $V_{12} = K_{12} Q_{12} > 1.0$

and ~~revealed the~~ indicated errors.

6/9/66

On 6/7/66 I setup 665,001 as a modification of the old Branchlet E (732.2 dated 11/4/63) See pp 159-160 of this notebook & also output folder.

One modification was to introduce transient E. Another was erroneous scaling of λ from Ec to post. compartment. I forgot the following important point. If the Ec source cpt. is regarded as having unity for the same size as cpt. 1, we have $Q_1 = V_1$ and $Q_8 = V_8$

But, for all other cpts $V_j = \frac{C_1}{C_j} Q_j$ $\boxed{K_j = \frac{C_1}{C_j}}$

Now $\lambda_{ij}/\lambda_{ji} = C_i/C_j$ see p.160

~~∴ For a fixed E value $\lambda_{12,8}$ should~~

also $\lambda_{i,8} \propto \frac{g_{i,8}}{C_8}$ and $\lambda_{j,8} \propto \frac{g_{j,8}}{C_8}$ for same E

But, if E_i is doubled as C_i is halved, and $g_{i,8}$ is halved, to make same amount of conduction charge

Then need $\lambda_{i,8} = \lambda_{j,8}$ (This makes initial current injection the same)

But, as was correctly provided in 732.213 but not in 655.001

$$\lambda_{sink,i} = \boxed{\frac{C_8}{C_i}} \lambda_{i,8}$$ to insure that the synaptic current is governed by voltage, not by Q.

K_i

error, see p. 180

665.102 results at right show that E in branchlet ⑫ of ②
causes larger v in ⑫ (about 5×)
but smaller v in ② ($\sim 5/12$) later
& hence " " in ① " ($\sim 1/2$) later

The area factor & E factor was $\frac{4}{32} = \frac{1}{8}$

Should also get input conductance or resistance

Next 665.103

do for ⑬ & ⑨ both attached to ③
$K=32$ $K=8$

6/13/66

Saw K, Phil & Bob on 6/10/66 re joint paper
Phil concerned with offered fiber-input resistance and coupling resistance
Bob has an outline
I proposed triggered postsynaptic rather than chemical

Re linearity. I pointed out & others were interested, that near linearity & deficient linearity are evidence against local response in dendrites.

6/13/66 got back 665.102 Branchlet GE see p160 & 172

Before T.C., had transient E to ② only

These answers subject to error, see p.180

~~in ① peak Q = .017865 at T = .19~~ ~~V = .017865~~

~~in ② peak Q = .03056 at T = .09~~ ~~V = .1222~~

~~in ⑫ peak Q = .0028257 at T = .15~~ ~~V = .09042~~

~~After T.C., had transient E to ⑫ only~~

~~in ① peak Q = .008754 at T = .27~~ ~~V = .008754~~

~~in ② peak Q = .01240 at T = .15~~ ~~V = .04961~~

~~in ⑫ peak Q = .01892 at T = .08~~ ~~V = .6054~~

See left.

Let $\tau\lambda_{ij} = 6.25$ where compartment $= \frac{1}{5}$ of total neuron surface area
$\simeq 10^4/5 = 2000\mu^2$

Contact area of knob cluster $\simeq 200\mu^2$ or $\frac{1}{10}$th

g_{jk} should be relatively large, because not core but to ~~neighbors~~ surrounding membrane

$\therefore$ let $\tau\lambda_{kj} = 25.$; let $g_{jk} = 25.$, $C_j = 1$, $C_k = 0.1$
$\tau\lambda_{jk} = 250.$ $R_j = 1 = G_j$;

also, let $g_K = g_A = \frac{g_j}{10}$ where $g_j/g_{ij} = 1/$~~25~~

then $g_{jk}/g_A =$ ~~62.8~~ $250.$ $\boxed{\frac{g_k}{C_k} = \frac{1}{\tau_k}}$

Setup 66~~5~~6.001 Rall Elect. Coupling.

chain of five

$V_K =$ cpt. 6

$\boxed{V_A \text{ is in cpt. } 8}$

$\lambda_{5,8} =$ ~~25.~~ $\lambda_{6,5}$ ← and $\lambda_{0,8} =$ ~~0.1~~ ~~25.~~ → $-\lambda_{5,8} - \lambda_{6,8}$ corrects for loss to 5 & 6

Cpt. 9 is dummy

$\lambda_{9,8} = 25.$
$\lambda_{8,7} = 25.$
generates for transient.

$\lambda_{6,8} =$ ~~-24.9~~ ~~and λ~~
$-\lambda_{6,5} + 0.1\,\lambda_{0,6}$

$\lambda_{6,5} = 25.$
$\lambda_{5,6} = 250.$

$\lambda_{0,6} = 1.0$ if normal membrane

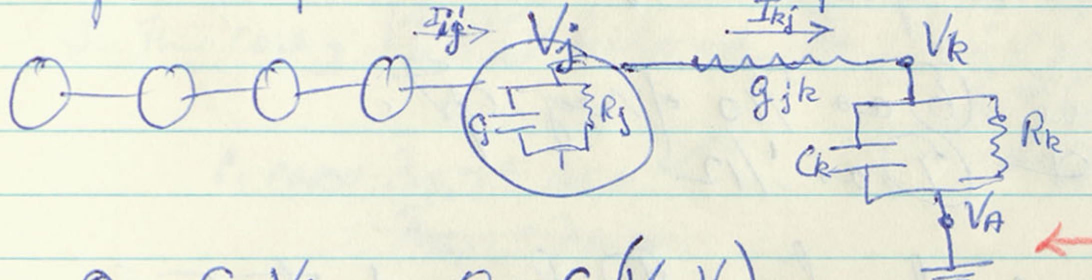
If increase $\lambda_{0,6}$ to 5. say, then $\lambda_{6,8} = -20.$ & $\lambda_{0,8} = -5.$

6/13/66 Talked with Phil on telephone

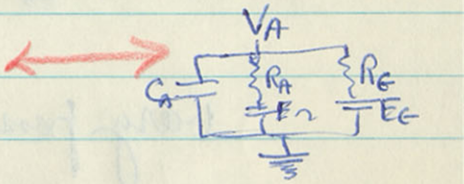
Must compute out transient aspects of coupling impedance.

D.C. argument holds only if coupling resistance very low compared to normal membrane & membrane time const.

Five Cpts Chain plus small membrane compartment (k)



treated with $E_r = 0$



$$Q_j = C_j V_j \qquad Q_k = C_k(V_k - V_A)$$

$$I_{kj} = g_{jk}(V_j - V_k) = g_{jk}\frac{Q_j}{C_j} - g_{jk}\left\{\frac{Q_k}{C_k} + V_A\right\} = \lambda_{kj} Q_j - \lambda_{jk} Q_k - g_{jk} V_A$$

$$\frac{dQ_j}{dt} = I_{ij} - I_{kj} - \frac{V_j}{R_j} = -\lambda_{jj} Q_j + \lambda_{ji} Q_i \overset{+\lambda_{jk} Q_k}{} + g_{jk} V_A$$

← use this in setup $g_{jk} = 25.$

$\rightarrow \lambda_{jk}\left(C_k V_A\right)$

where $\lambda_{jk} = g_{jk}/C_k$, $\therefore g_{jk} = \lambda_{jk} C_k$

cancel for effect on V_A

$\lambda_{kk} = \lambda_{jk} + \frac{g_k}{C_k}$

⑦

$$\frac{dQ_k}{dt} = I_{kj} - \frac{V_k - V_A}{R_k} = \lambda_{kj} Q_j - \lambda_{kk} Q_k + V_A\{\overset{.01}{g_k} - \overset{25.}{g_{jk}}\}$$

$$\downarrow$$

$$-\overset{Q_A}{C_k V_A}\left\{\lambda_{jk} - \frac{g_k}{C_k}\right\}$$

where $\lambda_{kk} = \frac{g_{jk}}{C_k} + \frac{g_k}{C_k}$

$\frac{1}{\tau}$ $\frac{1}{\tau}$

unless R_k smaller, g_k larger

If A flooded out, then

$$\frac{dQ_A}{dt} = I_{kj} - \frac{V_A}{R_A} - \frac{V_A - E_E}{R_E} = \lambda_{kj} Q_j - \lambda_{jk} Q_k - g_{jk} V_A - \frac{V_A}{R_A} - \frac{V_A + E_E}{R_E}$$

$$= \lambda_{kj} Q_j - \lambda_{jk} Q_k + G_E E_E - V_A(G_E + G_A + g_{jk})$$

$$\tau\frac{dQ_A}{dt} = \tau\lambda_{kj} Q_j - \tau\lambda_{jk} Q_k + \varepsilon E_E C_A - \underset{Q_A}{V_A C_A}\{\varepsilon + 1 + g_{jk}/g_A\}\left(K_9\varepsilon + \lambda_{0,7} + \frac{K_7}{K_6}\lambda_{5,6}\right)$$

In this problem, generate very large sharp transient in the presynaptic compartment (No. 7) with a large conductance change & see what this does to the postsynaptic membrane ~~compartment~~ (No. 6) & the chain of five compartments.

we have ⑥ as 1/10 of reg. cpt.
& ⑦ as 1/12

very passive loss from ⑥ from 1. to 5.
i.e. the subsynaptic membrane conductance.

The other thing that can be varied more is the ratio of g_6 to g_7 passive

& also the mag. of the excitatory conductance in ⑦

These correction dependence relations for $\lambda_{0,5}, \lambda_{0,6}, \lambda_{0,7}$ are needed because compartments 6 & 7 have rate terms ~~which~~ into them which are not really out of the others.

e.g. dQ_7/dt has terms $\lambda_{7,5}$ & $\lambda_{7,6}$ which are important to 7 (but are not really out of 5 & 6 in addition to what is already out of them)

6/14/66 Setup 666.101 with ~~two~~ chains of ⑤   ① → ⑤
⑪ → ⑮

ordinary $\lambda_{ij} = 6.25$

but $\lambda_{6,5} = 25.$ $\lambda_{5,6} = \overset{K_6}{10.} \times \lambda_{6,5}$ ✓

~~$\lambda_{16,15} = 25.$ $\lambda_{15,16} = \overset{K_{16}}{10.} \times \lambda_{16,15}$~~

$K_7 = K_{17} = 10.$ $\overset{10.}{K_6 = K_{16}}$

In this case, ⑦ & ⑰ become Q_A, and at first, $Q_A = C_K$
but later might be different.

∴ now $\lambda_{5,7} = \lambda_{5,6}$ ✓

~~$\lambda_{15,17} = \lambda_{15,16}$~~

$\lambda_{6,7} = -\lambda_{5,6} + \lambda_{9,6}$ ✓

~~$\lambda_{16,17} = -\lambda_{15,16} + \lambda_{0,16}$~~

~~$\lambda_{0,7} = \lambda_{0,17}$~~ →   ~~$\lambda_{0,7} = 1. + \overset{12.}{K_7} \times \lambda_{6,5}$~~

λ ~~$\lambda_{0,17} = 1. + \overset{12.}{K_{17}} \times \lambda_{16,15}$~~

Use cpt. 9 as dump, then ~~$\lambda_{9,7} = 1. + 12. \times \lambda_{6,5}$~~

~~$\lambda_{9,17} = 1. + 12. \times \lambda_{16,15}$~~

can be adjusted

Use $\lambda_{0,7}$ & ~~$\lambda_{0,17}$~~ to correct for $\lambda_{5,7}$ & $\lambda_{6,7}$ etc.   or $25. \times K_7$

Def. $\lambda_{0,7} =$ ~~$-\lambda_{5,7} - \lambda_{6,7}$~~ $+ 1. + 12. \times \lambda_{65}$

$-\lambda_{9,6}$

$\lambda_{7,5} = \lambda_{6,5}$ ✓ $\lambda_{7,6} = -\lambda_{5,6}$ ✓

~~$\lambda_{17,15} = \lambda_{16,15}$ $\lambda_{17,16} = -\lambda_{15,16}$~~

But then $\lambda_{9,5} = 1.$ and $\lambda_{0,5} = -\lambda_{7,5}$ ✓

$I_{12} = 1.$ $\lambda_{9,6} = 1.$ and $\lambda_{0,6} = -\lambda_{7,6}$ ✓

also $I_{10} = 2.718282$ $\lambda_{7,12} = \lambda_{0,9} \times Q_{11}$

$\lambda_{11,10} = 25.$, $\lambda_{0,11} = 25.$ $\lambda_{0,12} = -\lambda_{0,9} \times Q_{11}$

$\lambda_{9,7} = 12. \times \lambda_{0,9} \times Q_{11}$

Today, K. Frank said he thought my Part I manuscript plunged into quickly. Will discuss more tomorrow

665.013

6/17/66 Input resistance at ⑬ $\propto$ 2.77
also, the pecking order of steady state voltages comes out correctly.

For E transient to ⑨ get

	Cpt. No.	Peak Q	Peak Time	Peak V
	①	.00552	.60	.00552
	③	.01091	.24	.0873
E →	⑨	.0491	.13	.393
	⑬	.00243	.32	.0778

For E transient to ⑬ get

			estimate	
	①	.00535	(.42 ?) ~~.45~~	.00535
	③	.0138	.16	.1107
	⑨	.0068	.32	.0545
E →	⑬	.0192	.08	.616

peak in ⑬ is earlier, presumably because of larger λjj
larger " " " " input resistance

This causes second peak in ③ to be earlier and larger than 1st, but presumably smaller area under curve, because the peak in ① is slightly smaller and sig. earlier.

6/16/66

Yesterday wrote memo to modify & shift emphasis of Bob Burke's outline for joint EPSP paper.

Today, in checking over St.St. solution of 665.003, discovered error in $\lambda_{10,2}$, $\lambda_{2,10}$ ratio

see p.160

The program, as also used 665.002 p.174 and previous 732.2

had $\lambda_{2,10} = 1/2 \times \lambda_{1,2} = 4.$

$\lambda_{10,2} = 1 \times \lambda_{1,2} = 8.$

implying that 10 was twice as large as ②

& hence that ⑪ was 4X " " ②

This made too large a passive load.

In particular, it made my voltages come out wrong for the Kappas intended.

Today, corrected this error.

Also, St.St. solution was disturbed by $\lambda_{0,17} \neq 0$ making $\lambda_{17,9} \neq 0$

This ~~was~~ now made ~~originally~~ initially zero & set equal to 1.0 at zero time change.

New 665.013 encorporates corrections.

see results at left

axon resist. ↓ contact resist. ↓

6/21/66 refer back to conversation 6/17/66, The reason why R_A/R_C is important to whether EPSP is sensitive to postsynaptic hyperpol.

If have 10mV hyperpol, and if $R_C/R_A = 1/10$, Then resting hyperpol is 9mV across R_A and 1 mV across R_C. The 1mV across R_C becomes a resting leak contrib. to baseline from which EPSP rises. ∴ only 9mV is added to EPSP driving potential, when axonal ~~interior~~ goes to E_E

Note, assume $R_C >> R_E$, Then all of 10mV ends up across R_C, but only This minus resting drop across R_C adds to The EPSP driving pot. If $R_E \simeq R_C$, This will be reduced further to 5mV less resting.

But note, if terminal action potential is slow, as it was in 66a201, then there is less trouble with diphasic problem.

Here, we try to restore diphasic problem to test resistance ratios.

In order for fast action potential like transient in ⑦ should increase passive conductance of ⑦, This can be done in the dependence relation for $\lambda_{o,7}$ put in 7.

$$\frac{R_C}{R_A} = \frac{\lambda_{o7} \times C_7}{\lambda_{o6} \times C_6} = \frac{g_{o7}}{g_{o6}} = \frac{7 \times 5}{1 \times 10} = 3.5$$

after T.C. $\frac{7 \times 5}{.1 \times 10} = 35$

6/20/66

Got back 666.001 & 666.201
refer back to pp 176 & 178

666.001
$V_5 = Q_5$
$V_6 = 10. \times Q_6 = V_K - V_A$
setup new $V_{10} = V_6 + V_8$ i.e. $\sigma_{10,8} = 1.$
$\sigma_{10,6} = 10.$
also make Kappa 10 = 10, for plot,

Found peak at T = .43 in ①
T = .04 in ⑤ .081
& diphasic with neg peak at T = .25

peak of −.09 at T = .04 in ⑥
This is the drop across coupling membrane
which is neg for all values i.e. $(V_K - V_A) C_K$

After T.C.
5 times larger coupling conductance ($\lambda_{10,6}$)
got rid of diphasic features in ⑤ .098 peak now at T = .05
also peak in ① beyond T = .5
peak of −.086 at T = .04 in ⑥
which is only slightly less than before.
? is this due to input resistance?

666.201 peak V_7 was 0.84 at T = .05, gave $V_6 - V_7$ peak = −.64 at T = .06
peak ~~V_5~~ = .056 at T = .04, not diphasic by T = .2
but probably is later
maybe not because of slower trans in ⑦

after T.C.
with 5 × increase in $\lambda_{10,6}$
peak V_7 was 0.83 at T = .05, gave $V_6 - V_7$ peak = −.596 at T = .05
peak V_5 = −.073 at T = .1 & much slower altogether.

Also got back 666.001B ~~&~~ 666.202

666.001B has summer ⑩ for V_K that previous .001 did not have.
also got steady state input resistance at ⑥
comes out to 0.3694
also got plots, but scales not all suitable

Again got diphasic V_5 for normal membrane contact resistance.

& not diphasic when " " 5 times smaller.

V_K turns diphasic a little earlier than V_5
T=.12 T=.185

Whereas, with 5x smaller Contact resistance.
V_K not diphasic, because V_6 decays faster
i.e. it follows ⑧ better,
meaning that V_K follows 8 better also.

(6/27/66)

666.003 When $\lambda_{0,6}$ increased from 1. to 5.
steady state input resistance fell to 0.3218 at ⑥

		peak $\overset{Q}{\text{in}}$ ①		peak $\overset{Q}{\text{in}}$ ⑤	diphasic	reversed at
666.001&1B	$\lambda_{0,6}=1.$	.0023	at T=.43	.0808 at T=.04	yes	T=.18
	$\lambda_{0,6}=5.$	.0064	.70	.0977 at T=.05	no	
666.003	$\lambda_{0,6}=.5$	.00196	T=.4	.0789 at T=.04	yes	T=.16
	$\lambda_{0,6}=5.$	.00644 ~~.00478~~	.7 ~~T=.4~~	.0977 at T=.05	no	

6/21/66

Got back 665.014 which ran well except that missed early T values for ⑭ after T.C.

Setup 665.014 B to get this, also st. st. input resistance at ⑭ & replace ε at ⑤ with ε at ④

665.101 input resistance at ④ $16\times(.13375) = 2.14$

Here found st st. input resistance at ⑨ $\propto 8\times.28 = 2.23$

whereas previously at ⑬ $\propto 32\times.0865 = 2.77$

(refer back to 665.013)

⑭ $\xrightarrow[\text{6/22/66}]{32\times.118 \qquad p.179}$ 3.78

Here 665.014

	Peak Q	Peak time	Peak V
①	~.00358	~.75	~.0036
④	.0126	.20	.2023
ε → ⑤	.0337	.11	.53926
⑭	.00556	.28	.178

①	~.0032	~.70	~.0032
④	.013	.16	.208
⑤	.00913	.28	.146
ε → ⑭	.0198	.08	.633

①	~.0048	~.60	~.0048
ε → ④	.024	.10-	.384
⑤	.0148	.21	.237
⑭	.0094	.16	.30

Note, peak in ④ is earliest & largest with ε in ④ ~~4~~
next earliest with ε in ⑭ because closer & $\lambda_{14,14}$ very large
least early of these three with ε in ⑤

6/22/66 talked with Phil & Bob in afternoon

firmed up outline Started summary plots
see p. 190

6/23/66

see 665.101 below

Should check non-linear summation involving Branchlet, because this gets larger depol.

VF trans VS trans

Setup 615.551
615.554
{ for very fast ($\lambda_{17,13} = \lambda_{0,14} = 50.$) & very slow (5.)
for case of ε in ①
& ε in ④
to test time to peak for these cases, re plot of cpt # vs time to peak.

Setup 664.115
.125
.135
.145
Vary duration (4 durations) applied at ① of ten and at ⑯ alone.
↑ for uniform case

before noon refer back to pp. 71, 80, 112-114,

after noon

Plan 665.101 to work on MG, FDL problem using branching.
refer back to p. 47 & pp. 124, 131

slow MG alone $v_p \simeq 1.2/70 \simeq .017$; $T_p \simeq .6$
fast FDL alone $v_p \simeq 1.55/70 \simeq .022$; $T_p \simeq .2$

Expect to gain non-linearity by overlapping on cpt. ③ of branching system (p. 160)

Cpt 3 is $\frac{1}{8}$ of $\frac{1}{5}$ = $\frac{1}{40\text{th}}$ of total surface

Try first for separate EPSP. 3, 4 & 5 are 1/20th

Try ε peak = 1 in 3, 4, 5 for slow before T. C. $\lambda_{0,17}$

Try ε peak = 2 in 3, for fast after T. C. $\lambda_{0,18}$

These guesses are probably on low side; they are based on 665.013
.014

if not fast enough
put ε = 1 in 2 & 3

Now, go back to 666.202 & .203 which blew up whereas 666.201 did not.

These are the attempt to treat both presynoptic and postsynoptic conductances.

Only clue to blowing up of .202 & .203 is that purposely made K_7 smaller & E larger, but possibly there is a lost card or something of this sort due to gremlins. Hoping it is not gremlins, restore $K_7 = 12.$ and E as before, in .201 but make E faster with rate consts of 50.

The purpose of all this is to check hunches about the effect of $R_A > R_C > R_E$ manipulations upon transients under hyperpol.

with $K_7 = 12.$ $R_7/R_6 = 12/10. = 1.2$

however, when $\lambda_{9,6}$ becomes 5., get $\frac{R_7}{R_6} = (1.2)(5) = 6.$

If this works, then try St. St.

As a precaution, for st.st., make $\lambda_{0,9} = 0$ for initial set

Then for zero T.C. & for 1st T.C. set $= 25.$

Look to see whether st.st. in ⑦ is pos or neg.

was neg in .202 & .203 but not sure why.

666.204

form late 6/23/66

6/23/66

Thinking about 666.001 — 666.003 see pp. 182-183 & p. 176

Here, have voltage source from axon assumed, but explicitly include both resistance & capacitance of the contact membrane.

If there were no contact capacitance to consider, then could setup just the way I setup E, namely, synaptic current $\propto (V_A - V_K)$. What the above calculations have done is to imply that contact capacitance is always 1/10th of ordinary compartmental capacitance, and the contact resistance has been decreased by factor of 5, and also, in 666.003, increased by factor of 2. What happens is that a bucking potential developes across contact impedance, and $V_K = (V_A + C_c Q_c) < V_A$ because Q_c is neg.

With large R_C, time constant is large enough that Q_C decays more slowly than V_A, & V_K becomes diphasic.

With small R_C, time constant small enough to permit Q_C to decay fast enough to be smaller (abs. value) than V_A; then V_K remains pos.

When V_K is diphasic, V_5 is also diphasic but V_1 is not, it is briefer than control.

A check on this intuitive reasoning is that if Cpt. 6 is made much smaller, so that C_c is smaller, but R_C is compensatorally decreased ($\lambda_{0,6}$ increased), then V_K should become more nearly proportional to V_A, because $C_c Q_c$ becomes very small.

$\lambda_{5,6} = 625.$

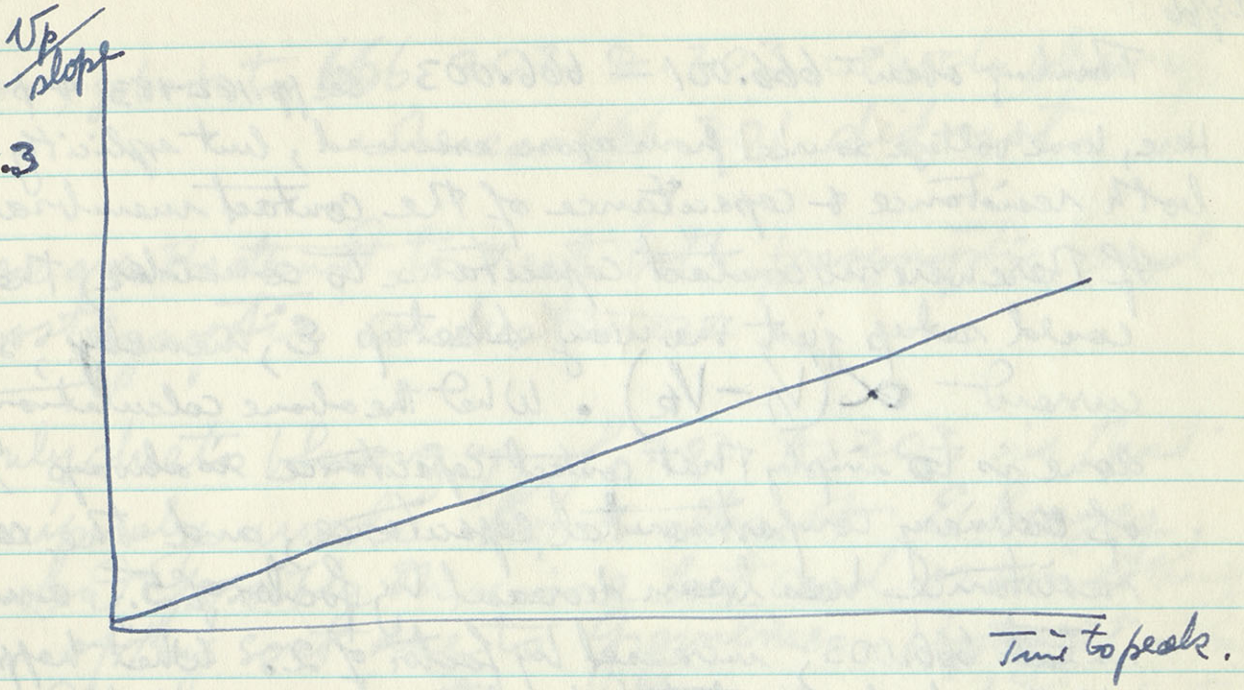
∘∘ Setup 666.004 with Kappa 6 = 50.

$J_{10,6} = 50.$

late 6/23/66

$\lambda_{0,6} = 5.$ before T.C., 25. after T.C.

Fig. 3



see where variable duration & squares fit here

6/24/66 morning

Put in 615.501 very fast trans (50.) for uniform Σ single cpt.

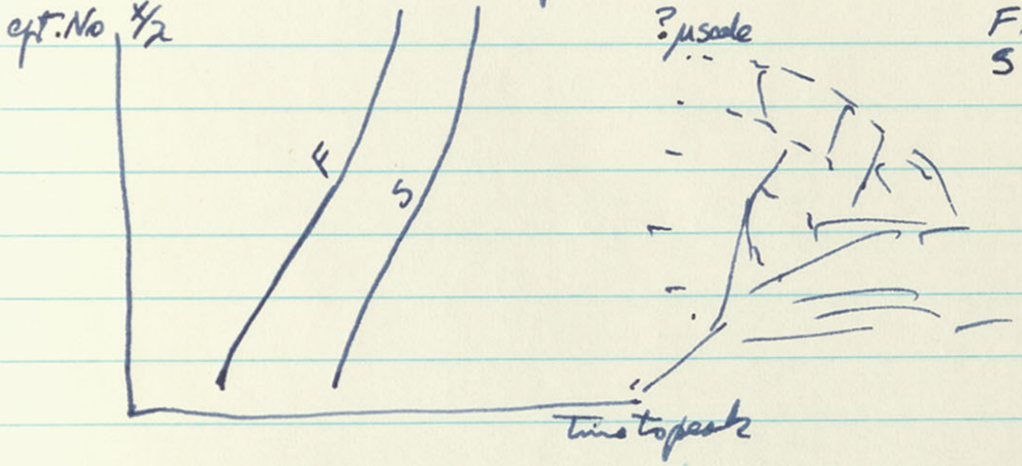
and 615.042 $Z_m = 4.$ with Σ at ④

① ⟷ ④ is 3×.4 = 1.2λ

Compare with ① ⟷ ⑦ 6×.2 = 1.2λ

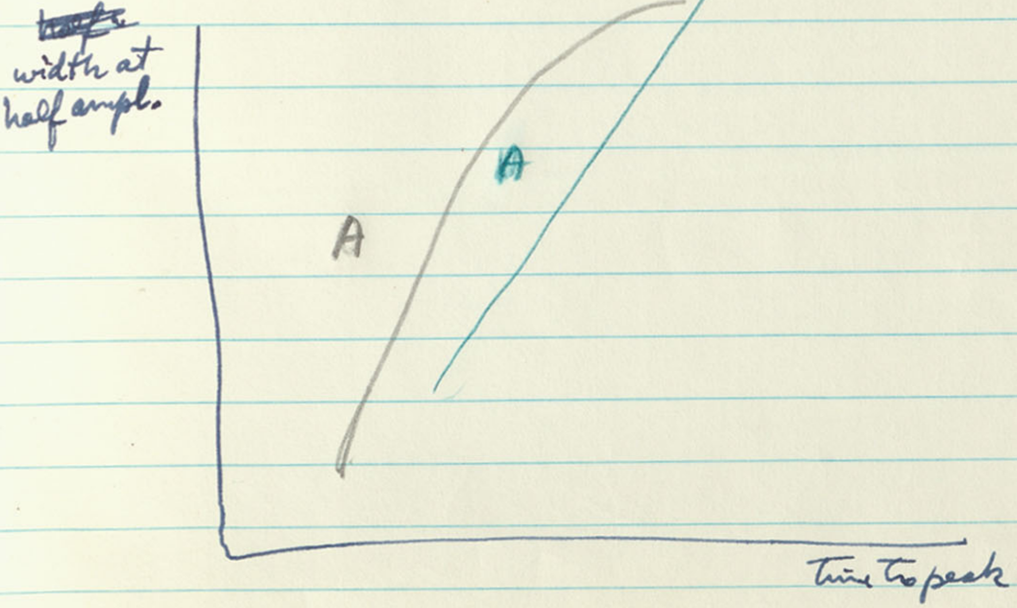
6/24/66 Return to outline, Phil had typed up 6/23/66 and to plots I prepared late 6/22/66

Plots actually stimulated to computations & setup yesterday. There are three plots.



	λ
F means fast trans	25.
S means slow trans	10.87
decided to setup VF	50.
VS	5.

Fig. 1



note that all uniform cases have larger WHA/TP ratio

Should see where Four Σ duration results fit

also decided to do 4 durations at ① & for all

Fig. 2

Rosenthal

phoned 3/9/66

Cable equations

645.1

fast runs.

Belongs at p. 113
Book 8

	①	②	③	④	⑧	⑩
falling ½ max	.33	.48	.663	.858	1.74	1.88
peak	.11	.16	.22	.29	.73	.86
Δ	.22	.32	.44	.568	1.01	1.02
peak	.11	.16	.22	.29	.73	.86
rising before	.036	.062	.092	.125	.32	.24
Δ	.064	.098	.128	.165	.41	.62
Ratio	3.44	3.27	3.44	3.44	2.47	1.64

↑

$\frac{\text{peak to ½ down}}{\text{½ up to peak}}$

time of	664.414	664.424	664.434	664.444
½ down	>.5 ~.7	.845	1.02	>~1.4
peak	.23	.30	.46	.83
½ up	.105	.155	.235	.355
	$\sim\frac{.47}{.125}$	$\frac{.545}{.145}$	$\frac{.56}{.225}$	$\sim\frac{.57}{.47}$
Ratio =	3.75	3.75	2.48	~1.2

why $x = \frac{\frac{1}{2}(V_1 - V_2)}{(1 - \frac{1}{2}(V_1 + V_2))}$

646.150

$x = \frac{.00955}{(.1662)} = .0575$

Whereas $.00955 + (.044)(.8338)$

$.0367$

$x = .04625$

646.140

$x = .0323$

$.0326$

$.0649$

646.122

$x = .142 + (.1622)(.174)$

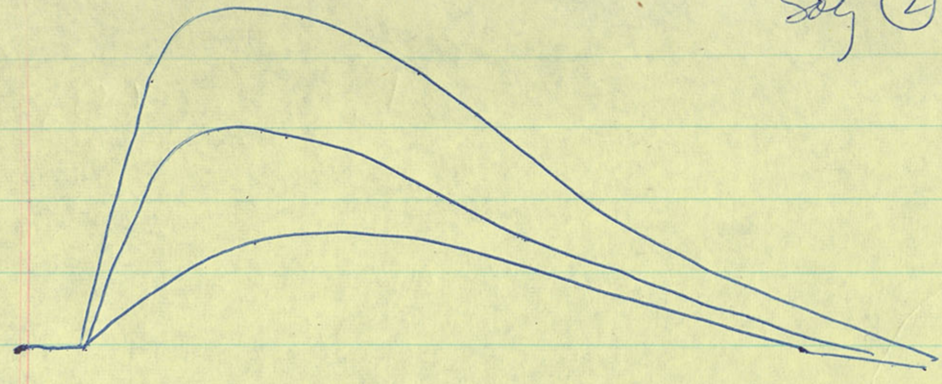
$+ .0283$

$.170$

Bob Burke's FDL, MG result is most easily explained if the slow EPSP (MG) actually has some J in the early part. This would knock the early FDL, but not the late.

12/22/65

Try this with a
pair of short chain
say ② vs ④



Slow (MG) - Ampl. 1.2 mV
Time to peak 2.95 msec .66 to .75 τ
mV/msec 0.75
mV/msec/mV 0.80 ~4 per τ

Fast (FDL) Ampl - 1.55 mV
Time to peak - 1.07 msec .2 to .25 τ
mV/msec - 2.1
mV/msec/mV - 2.08 ~8 to 10 per τ

both (summated PSP) - Ampl. 2.26 mV
Time to peak 1.10 msec
mV/msec. $\frac{x}{1.10} = 1.77$?
mV/msec/mV - 1.77

1/20/66

Distinguishing synaptic potentials computed for different distributions of synaptic conductance change.

Distinguishing Synaptic Potentials Computed for different spatial distributions of synaptic conductance change.

1/18/66 1:45 PM.

Check with Lew. or C. Bishop about travel request.

Attended Jose's lecture this morning & took notes.

Interesting

Talking after lunch with Jose

Several ~~interesting~~ points came out

(1) Equivalence classes, as for example Real Numbers
Each object in the real number system represents a class of many different objects which may be obtained in many different ways, such as limits of different sequences.

(2) This point came ~~out~~ of non-uniqueness of a fundamental solution of a system of linear homog. diff. eqns. (cf. general of second order diff eqn). Point is that there is a non-uniqueness, but math. focus is upon invariances, the equivalence class of all such fundamental solutions & the fact that they are all characterized by the same eigenvalues & ~~same canonical~~ are the same when transformed into canonical form.

(3). Then I made point about my not attempting to prove that compartmental solutions converge to P.D. Eq BVP, but that I am content to solve the modified physical problem.

Jose's comment to this is that there is much modern math that follows a somewhat analogous approach.

Briefly — convergence in the domain of continuous fcns may not be required anyway.

One may be satisfied with other classes of convergence defining other classes of solutions.

Thus. Sobolev defines weak solutions somewhat as follows

Whereas normally we seek a soln which satisfies $L(u) = 0$

we may seek $L(u_j) = \epsilon_j$

Such that u_j is a sequence for which $\epsilon_j \longrightarrow 0$

The limit of u_j is called a weak solution ~~which~~ but this limit may not, itself be a strict soln of the original problem.

In an other direction, functional analysis finds that there are solutions in the integral sense which are not strict solns of the differential equations. In other, the differential equations often demand more of a soln. than we really need, that is in the sense of continuity and differentiability.

Apparently, before the time of Newton & Leibniz, there was almost an even balance between continuous & discrete approaches to mathematics. Following them, the balance swung heavily to the continuous & tremendous developments took place.

However, physics & now the computer & other factors have heightened interest in getting away from the restrictions of the continuous esp. since these are often unrealistic anyway. To me, this is a valuable insight because (as Jose intended by his remarks) this reinforces the notion that I used ~~of~~ ~~getting around~~

The physics gets around mathematical difficulties by choosing appropriate physical assumptions.

& certainly, in biology & much of physics, we do not need the artificial idealization of perfect continuity. We are usually concerned with quantities that are measured as averages (integrals) over finite vol & finite time & the math. need not satisfy more resolution than this. The trick has been to develop rigorous mathematics that gains by freeing itself of the limitations of a fictitious resolution that is too high.

Functional Analysis is an example.

Sobolev's Weak solutions are another.

Jose commented that all this has the disadvantage of crushing the dream of unification thru mathematics.

I commented upon Bohr's complementarity principle.

He commented that one might still achieve a more general math in which all these would be various special cases that could be related as equivalence classes.

The point is, however, that there exist many mathematical solutions which do not converge, but rather, oscillate wildly when examined at very high resolution, but which converge perfectly O.K. when examined at lower resolution which gives the integral over finite ~~vol. 6~~ region.

12/27/65

Predictions and Generalizations from the computed effects of synaptic conductance change at different soma-dendritic locations.

~~Dendritic location~~

Effect of dendritic location

Effects of the

Comparisons between computed synaptic potentials

Synaptic potential computations for various

Characteristics of synaptic potentials computed for various soma-dendritic distributions of membrane conductance change.

(Analysis or Comparison) of Computed synaptic potentials for

Advantage of expts. with mathematical model is that we can obtain answers to questions that are very difficult to ask experimentally. Generalizations & insight can be obtained.

Previously showed what happens when a particular (square) excitatory conductance change is assumed to occur at different locations.

Conclusions

12/17/65

~~As soon as one discards the old dogma synoptic~~ activity in the

Many new and interesting questions arise as soon as one discards the old dogma which held that synoptic activity delivered to the dendritic ~~periphery could~~ surface of a neuron have no effect

---

Previous theoretical studies have ~~shown that~~ provided ~~computed examples of the~~ quantitative comparisons of ~~examples~~ simulated ~~excitatory~~ synaptic potentials added better when first one was made latter 12/22/65

Tom I a. Impedance change measured with ipsp
b. delayed or absent ΔZ with epsp.

Phil II. AR present
Variable change in epsp with polarizing current
also effect on specific rise rate of epsp.

Bob III Interaction epsp & ipsp — variable epsp
Timecourse of evoked & stim potentials
minis. – homogeneous, heterogeneous

believes consistent with conductance change

Wil IV Expts with model.
effects of dendritic location for different conductance time courses

Joint V Put together motoneurone data & model knowledge.

Bargraph showing epsp summation usually 95% linear

for summed amplitudes up to 8mV max

It became more linear when the sharp one was made latter.

fast one in ③
slow one in ⑥

range 4 to 8 mV
for summed epsp.

∴ I should do some epsp .05
to check linearity of same
site & different sites.

③ or ⑧ for slow trans Σ

perhaps ③ or ⑥ ?